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Highlights

- Synergic Anticancer Activity Extracts of Ziziphusa Mauritiana
- Assessment of Substance Abuse
- Antihypertensive and Antiatherogenic

Discovering Thoughts, Inventing Future

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Synergic Anticancer Activity of Different Extracts of *Ziziphus Mauritiana* and *Punica Grantum* L on the Inhibition of Hela Cell Proliferation and Tumor Growth in EAC Bearing Mice

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Abstract- In consideration of the synthetic chemicals chemotherapy has induced obnoxious hazards, there is a ubiquitous tend towards the natural resources, which are remedially potent and affordable for the poor people. Development of phenolic compounds or extracts has become a major area medical research due to their cancer preventive effects through induction apoptosis and prevention of oxidative stress associated cancer. The present scrutiny was designed to investigate the synergic anticancer effect of *Punica grantum* L and *Ziziphus maritiana*. The ethanol extract of combination of both plants were found to be the most effective in BSL and trypan blue assay, also stimulated caspase-8 and-9 protease by fold increase in Ac-IETD-pNA. The expression of P_{53} in cytoplasm and nuclei and the increase of TdT in the nuclei of carcinoma cells in mice treated while Bcl_2 expression was declined. Consequently, the synergic anticancer activity of ethanol extract of combination of both plants was proved.

Keywords: *anticancer activity, apoptosis, carcinoma cells, Punica grantum L, Ziziphus maritiana.*

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SYNERGICANTICANCERACTIVITYOFDIFFERENTEXTRACTSOFZIZIPHUSMAURITIANAANDPUNICAGRANTUM LONTHEINHIBITIONOFHELA CELLPROLIFERATIONANDTUMORGROWTHINEACBEARING MICE

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Synergic Anticancer Activity of Different Extracts of *Ziziphus Mauritiana* and *Punica Grantum* L on the Inhibition of Hela Cell Proliferation and Tumor Growth in EAC Bearing Mice

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Abstract- In consideration of the synthetic chemicals chemotherapy has induced obnoxious hazards, there is a ubiquitous tend towards the natural resources, which are remedially potent and affordable for the poor people. Development of phenolic compounds or extracts has become a major area medical research due to their cancer preventive effects through induction apoptosis and prevention of oxidative stress associated cancer. The present scrutiny was designed to investigate the synergic anticancer effect of *Punica grantum* L and *Ziziphus maritiana*. The ethanol extract of combination of both plants were found to be the most effective in BSL and trypan blue assay, also stimulated caspase-8 and-9 protease by fold increase in Ac-IETD-pNA. The expression of P_{53} in cytoplasm and nuclei and the increase of TdT in the nuclei of carcinoma cells in mice treated while Bcl_2 expression was declined. Consequently, the synergic anticancer activity of ethanol extract of combination of both plants was proved.

Keywords: anticancer activity, apoptosis, carcinoma cells, Punica grantum L, Ziziphus maritiana.

I. Introduction

Cancer is a multi-process disease integrating environmental, chemical, physical, metabolic, and genetic factors which play a direct and/or indirect role in the induction and retrogression of cancers. Strong and consistent epidemiology declaration implies a diet with high consumption of antioxidant rich fruits and vegetables significantly reduces the risk of many cancers, suggesting that certain dietary antioxidants could be effective agents for the precaution of cancer incidence and mortality. These agents present in the diet are a very promising group of compounds because of their safety, low toxicity, and general acceptance (Fresco et al., 2006). Accordingly, in the last few years, the identification and development of such agents has become a major area of experimental cancer research. Phenolic compounds constitute one of the most numerous and ubiquitous group of plant metabolites, and are an intrinsic part of the human diet. It was found that besides their primary antioxidant activity, this group of compounds exhibit a wide variety of biological functions which are mainly related to modulation of carcinogenesis. Various *in vitro* and *in vivo* systems have been exerted to determine the anticarcinogenic and anticancer potential of these natural phenolic compounds or extracts. For example, *invitro* study of berry extracts and isolated polyphenols from strawberry including anthocyanins, kaempferol, quercetin, esters of coumaric acid and ellagic acid, were exhibited to inhibit the growth of human oral (KB, CAL-27), breast (MCF-7), colon (HT-29, HCT-116) and prostate (LNCaP, DU-145) tumor cell lines in a dose-dependent manner with different sensitivity between cell lines (Zhang et al., 2008; Seeram et al., 2006). Similar results have also been recited in several cell system with wine extracts and isolated polyphenols (resveratrol, quercetin, catechin, and epicatechin) (Damianaki et al., 2000; Kampa et al., 2000), tea extract and major green tea polyphenols (epicatechin, epigallocatechin, epicatechin-3-gallate, and epigallocatechin-gallate) (Zhang et al., 1999; Weisburg et al., 2004; Nichenametla et al., 2006), despite the effective concentrations depend on the system and the tested substances. Other phenolic extracts or compounds profoundly studies are from olives, legumes, citrus, apples, and also curcumin from spice turmeric. Moreover, *in vitro* studies on cancer cell lines, abundant *in vivo* experiments have also been executed to certify the antitumor efficacy of plant food-derived phenolic extracts or compounds with tumor prevalence and multiplicity (e.g., number of tumors per animal) as endpoints (Yang et al., 2002; Lambert and Yang, 2003; Gerhauser, 2008; Thomasset et al., 2009). The animal models frequently employed are either chemically, genetically, or ultraviolet light-induced tumor, as well as xenograft models, including colon, lung, breast, liver, prostate, stomach, esophagus, small intestine, pancreas mammary gland and skin tumors. (Lalaet al., 2006) investigated the chemoprotective activity of anthocyanin-rich extracts (AREs) from bilberry, chokeberry, and grape in Fischer 344 male rats treated with a colon carcinogen, azoxymethane (AOM). After 14

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weeks, rats on ARE diets had significantly fewer colonic aberrant crypt foci (ACF) when compared with the control group. Moreover, rats fed bilberry ARE had 70% fewer large ACF compared with rats fed the control diet, indicating significant chemoprevention. Chokeberry-fed rats had a 59% reduction in large ACF, whereas the reduction was only 27% in rats fed grape ARE. The authors wound up that AREs from bilberry, chokeberry, and grape notably prohibited ACF formation induced by AOM. One more investigation by (Ding et al., 2006), cyanidin-3-glucoside (C3G), the major anthocyanin in blackberry, was surveyed for the potential ability to inhibit 7,12-dimethylbenz[a]anthracene (DMBA)-12-*O*-tetradecanolyphorbol-13-acetate (TPA)-induced skin papillomas in animal skin model. The results revealed that treatment of the animals with C3G (3.5 μM, topical application, twice/week) decreased the number of tumors per mouse at all exposure times. After 20 weeks of TPA promotion, a greater than 53% inhibition of papillomagenesis by C3G was observed. Keeping above in view, the present study was taken up to predict potential antitumor effect of aqueous, ethanol and chloroform seed extracts of *Ziziphus mauritiana* and *Punica grantum* L in combination (which contain phenolic componds) to evaluate the synergic effect of both plantsin Hela cells for *invitro* study and EAC tumor bearing mice for *invivo* study as there is no previous anticancer activity reported for the combination of the two plants.

II. Materials and Methods

a) Plant material and Preparation of extracts

The seeds of *Punica grantum* L (*Punicaceae*) and *Ziziphus mauritiana*(*Rhamnaceae)*were collected from Udupi District, Bangalore, Karnataka State, India and authenticated by Green Chem of India, Bangalore, Karnataka, India, a voucher specimens (NRI-COP-204; NRI-SOP-309) for *Punica grantum* L and *Ziziphus mauritiana* respectively were preserved for future references. The seeds were rinsed with water for the evacuation of adhering material and sun dried. Seed powders were prepared mechanically, passing through sieve # 40 and stowed in sealed container. The seed powder (1kg) was extracted in a soxhlet with hexane (4000ml) for 6h for the segregation of fatty compounds. The hexane extract was discarded and residues were successively extracted with distilled water, ethanol and chloroform (3200ml each) for 8h each. The extracts were filtered and concentrated under vaccum (Buchi, Switzerland) to get concentrated extracts (60g), which was dried in vaccum oven and stored in a desiccator.

b) Chemicals

Apotarget caspase colorimetric protease assay kit was purchased from Invitrogen Company. (TUNEL) assay kit and biochemical assay kits were bought from Roche Molecular Biochemicals Company and Sigma-Aldrich Company respectively. Trypan blue was obtained from Bio-tech Pvt Ltd (India), All other chemicals were analytical grade.

c) Tumor cells line for caspase 8 and 9 assay

The Hela cell line (Cervical cancer) was obtained from National Center for Cell Science, Pune, India. Cells were grown and maintained in DMEM medium which contained 10% fetal calf serum, penicillin (100units/ml) and streptomycin (100μg/ml)., PH 7.4. The cell culture was maintained in carbon dioxide incubator at 37^{0C} with 90% humidity and 5% CO_2.

d) Tumor cell line for in vitro cytotoxic test and invivo study

EAC cells were obtained by Amala Cancer Research Center, Thrissur, Kerala, India and were maintained by weekly intraperitonial (i.p) inoculation of 10^6 cells/mouse in the laboratory. Ehrlich Ascites Carcinoma (EAC) cells maintained in the peritoneal cavity of Swiss albino mice were collected from an animal having 7 days old ascetic tumor by aspirating the ascitic fluid in sterile isotonic saline. The viable EAC cells were counted (trypan blue indicator) under microscope. A fixed number of viable cells 10^6 cells were inoculated into the peritoneal cavity of each recipient mouse.

e) Animals

Healthy male adult Swiss albino mice: BALB/cJ, with age of 3 months and weighing 25±5 g was obtained from the Drug Control Laboratory (DCL), Bangalore. that were housed in well ventilated cage and animals had natural day and night cycle with temperature between 25±3°C. The animals were housed in large spacious hygienic cages during the course of the experimental period. The animals were allowed free access to standard laboratory cube pellets and drinking water *ad libitum.* The study protocol was approved by Institutional Animal Ethics Committee (IAEC), Visveswarapura Institute of Pharmaceutical Sciences, Bangalore. (Registration No: 152/1999, renewed in 2012).

f) Brine shrimp lethality (BSL) bioassay

The brine shrimp (Artemiasalina) eggs were bought from Brine Shrimp Direct, Ogaden, UT, USA. The assay was accomplished for the investigation of cytotoxicity of the selected extracts. The procedure and method was pursued as illustrated by (Meyer et al., 1982).The chamber was divided into two equal parts. Aeration was given in both the compartments. One part was lighted up with a bulb (60 W), while the other was darkened. Brine shrimp eggs were scattered in the dark side and incubated at room temperature for 48h. As the hatching occurred, the nauplii were swum towards the illuminated side, where they were compiled by a Pasteur pipette. Samples of the extracts were prepared by dissolving 5mg of extract in 5ml of DMSO to get 500 ppm stock solution and further diluted with sea water to

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get the required concentration (10, 50, 100 and 150 μg/ml). 5-Flourouracil (5-FU) was used as standard (1, 10, 25 and 50 μg/ml). Dried vials were taken and ten shrimps were transferred in each vial and then volume was made up to 5ml with sea water. A drop of dry yeast suspension (3mg in 5ml sea water) was added to each vial as food for shrimps. For each concentration test was done in triplicate. Control vials were prepared by adding equal volumes of distilled water. The vials were sustained under illumination. After 24h survivors were counted, by using 3× magnifying glass and the percentage of deaths (% Mortality) and IC_{50} value were calculated by using Finney Computer program.

g) In-vitro Cytotoxicity (Trypan blue dye exclusion method)

In-vitro cytotoxic activity was accomplished using the Trypan Blue cytotoxic assay. Concisely, ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana* was used for the preparation of the stock solution (1000 μg/ ml) in Phosphate buffered saline. Serial dilutions (200, 20, 2 and 0.2 μg/ml of sample solution) were prepared in PBS. Sample solutions (200μl) were placed in tubes. The volume in all the tubes was made up to 800 μl with PBS (Phosphate buffered saline). 100μl of EAC with a concentration of 10^6 cells/ml of Phosphate buffered Saline was added to the tubes. A control having solvent alone was also prepared. Incubate at 37^{0C} for 3 hours and add 100 μl of trypan blue to all test tubes. Ascitic tumour cell counts are done in a Cell Counting machine (Cedex, Roche) using the trypan blue dye exclusion method. Results were expressed as percentage cell viability (Saluja et al., 2011).

h) Caspase assay

Caspase activity was governed by using Apotarget caspase colorimetric protease assay sampler kit (Catalog number: KHZ1001; Invitrogen, USA). HeLa cells were treated or without ethanol extract of ZP, 5-FU for 24 h. The cells were then accumulated, rinsed in PBS and lysed in 50 μl of lysis buffer on ice for 10 min. After centrifugation, the supernatant containing 150 μg proteins were incubated with 200 μM Caspase-8 (AC-IETD-pNA) and Caspase 9 (Ac-LEHD-pNA) substrates in reaction buffer at 37^{0C} for 1h. The levels of released pNA were measured with microplate reader (Fluostar optima, BMG Labtech, Germany) at 405 nmwavelength. The fold-increase in caspase 8 and caspase 9 activities was determined by direct comparison to the level of the untreated control, which was considered as 1 (Kumar et al., 2014).

i) DNA isolation from Ehrlich Ascites Carcinoma Cells

The EAC cells assembled from treated and untreated animals were used for DNA fragmentation assay using the modified method of (Jun-yaet al., 2002). Cells were rinsed twice in 800 μL of PBS and pelleted. Pelleted cells were lysed in 600 μL ofLysis buffer (10 mMTris-HCl buffer, pH 8.0, 10mM EDTA and 0.2% Triton X-100) for 10 minuteson ice. The lysate was centrifuged at 6000 rpm for20 mins. Then, the supernatant was extracted with1000 μL of PCIAA (Phenol – chloroform – Isoamyl alcohol solution, 25:24:1). The mixturewas then centrifuged at 6000rpm for 20 mins andthe upper layer decanted off and precipitated with50 μL of 3M NaCl and 1000 μL of cold ethanol at -200C overnight. After drying, the isolated DNAwas dissolved in TE buffer. Contamination byRNA was removed by incubation with 40 units of RNase at 370C for 30 minutes.

j) DNA fragmentation assay on 2% agarose gel

Loading buffer was added, and (fragmented) DNA electrophoresed on 2% agarose gel in TBE(40 mMTris, 20 mM Boric acid, 1mM EDTA) at100 V for 45 minutes and visualized by EtBrstaining.

k) Treatment schedule

Experimental tumor was induced by inoculation of $1x10^6$ Ehrlich ascites carcinoma (EAC) cells from the tumor bearing mice aseptically. Group 1 mice (n=6) served as normal control, group 2 mice (n=6) were EAC control. Group 3 mice (n=6) received standard drug 5-Flourouracil 20 mg/kg b.w, i.p., whereas group 4, 5 and 6 (n=6) mice were administered, orally, aqueous, ethanol, chloroform extract of combination of both plants (ZP) of 200 mg/kg b.w, respectively, for nine days. Animals from each group were sacrificed, liver homogenate was collected and Biochemical parameters were estimated.

l) Biochemical parameters

Abundant laboratory surveys have been suggested in the appraisal of liver dysfunction. For assessment of drug induced hepatotoxicity, liver function tests were carried out and values obtained for treated groups were correlated with the normal value. From among the host of liver function tests, the following battery of blood tests namely bilirubin, SGOT, SGPT, ALP and protein levels were done. (Pain et al., 2003)

m) Histological of plasma and immunohistochemical examination

The immunohistochemical investigations were done by staining with haematoxylin and eosin. Sections mounted onto positive charged slides were applied to distinguish the Bcl-2 and p53 reactivity or apoptotic cells by using the TUNEL assay (Gao and Zhou, 2005). Streptavidinbiotin or avidin-biotin peroxidase (ABC/ HRP) was used and bound antibody complex was visualized by the reaction of 3, 3`-diaminobenzidine (DAB) substrate and counter stained with haematoxylin.

n) Statistical analysis

The data were expressed as mean ± S.E.M (n=3 for *invitro* study n=6 for *invivo*). The statistical analysis involving five groups was performed by means

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analysis of variance (ANOVA) followed by Dunnett's post hoc test where the difference was considered significant if $p < 0.05$.

III. Results

a) Brine shrimp lethality bioassay

Ethanol extract of combination of *Punica grantum* L and *Ziziphus Mauritiana* was found the most effective with lesslethal concentration LC_{50}. 5-FU showed IC_{50}: 1.98 μg/ml as standard drug.

Table 1: Effect of ethanol, aqueous and chloroform extract of combination of *Punica grantum* Land *Ziziphus mauritiana* on brine shrimp lethality bioassay. All the values are mean ± S.E.M of three samples.

EXTRACT	% Mortality after 24 h				LC_{50} (μg/ml)
	10 (μg/ml)	50 (μg/ml)	100 (μg/ml)	150 (μg/ml)	
Control	0.00	0.00	0.00	0.00	--
ZP (E)	80.65	92.21	98.66	99.83	2.03
ZP (Aq)	64.08	83.34	97.32	98.22	7.83
ZP (Ch)	12.32	26.00	35.32	45.98	378.43

ZP (E): Ethanol extracts of combination of Punicagrantum L and Ziziphus Mauritiana. ZP (Aq): Aqueous extract of combination of Punica grantum L and Ziziphus mauritiana. ZP (Ch): Chloroform extract of combination of Punica grantum L and Ziziphus mauritiana.

b) In vitro cytotoxicity in EAC cells (Trypan blue exclusion)

It is evident from the results in figure 1 that the death rate of Ehrlich ascites carcinoma (EAC) cells *in-vitro* increases with the concentration ofethanol extracts of combination of *Punica grantum* L and *Ziziphus mauritiana*. Ethanol extracts of combination of *Punica grantum* L and *Ziziphus mauritiana* at concentrations of 0.2, 2, 20, 200 μg/ml caused mortalities of 10.6, 27.9, 45.1 and 82.5 % respectively in Ehrlich ascites carcinoma cells.

c) Caspase 8 and 9 activity of ethanol extract of combination of Punica grantum L and Ziziphus mauritiana

Figure 2 and 3 show caspase 8 and 9 protease activity of ethanol extract of combination of *Punicagrantum*L and *Ziziphus mauritiana*. It is observed that ethanol extracts of combination of *Punica grantum* L and *Ziziphus mauritiana* significantly stimulated caspase 8 and 9 protease activity. Cells showed a 17.7-fold increase in Ac-IETD-pNA (Caspase 8) and 18.9-fold increase in Ac-LEHD-pNA (Caspase 9) cleavage at dose of 100μg/ml.

d) DNA fragmentation

Figure 4 revealed the fragmentation of DNA extracted from the ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana* treated cells in agarose gel electrophoresis. The DNA from the control was perceived to be complete and unbroken although the fragmentation pattern of 5- Fluorouracil-treated cells was more intense that compared to the pattern of ZP (E)-treated cells.

e) Biochemical parameters

There were significant increase in the level of ALP (Alkaline phosphatase) and also in level of both transaminases SGPT (Serum glutamic pyruvic transaminase) and SGOT (Serum glutamic oxaloacetic transaminase) in EAC untreated group while their values stayed in the normal range in ZP (E), (100mg/kg) treated group, redolent of its efficiency with less toxic effect compared with the standard as seen in Figes 5-7 respectively. The levels of protein andbilirubin didn't differ significantly from normal in ZP (E) treated group which were depicted in Figs 8 and 9 accordingly.

f) Histological and immunohistochemical effects in EAC bearing mice

Figure 10 (A, C and E) showed the highly proliferated rate, abundant basophilic and dark stained cytoplasm and moderate sized nuclei of EAC cells of control mice. Many dividing cells are depicted in (Figure 10 E). The number of EAC cells were decreased and also some cells were degraded due to the treatment with ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana* at dose of 100mg/kg (Figure 10D). Figure 10 (B, D, F) illustrated phenotypic apoptotic signs including irregular shape, cell shrinkage, plasma membrane blebbing, cytoplasmic azurophic lytic vesicles, fragmenting nuclei and apoptotic bodies. Figure 11 A signified the decreasing in density of Bcl-2 in cytoplasm of EAC cells treated with ZP (E) extract as compared with control. EAC treated with ZP (E) revealed considerably upgrading of p53 in cytoplasm and nuclei and TdT in nuclei compared with untreated control mice (Figure 12 and 13).

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IV. Discussion

The advanced stage of cancer can be controlled by synthetic compounds, but almost all of these compounds display normal tissue toxicity with unenviable side effects. Consequently, the research for safe compounds that may have anticancer efficiencies should be evaluated. Different extract of combination of *Punica grantum* L and *Ziziphus Mauritiana* as natural product was tried out to assess biochemical parameters as consequence of getting better result from ethanol extract of combination of both plant, this extract was surveyed for caspase activity, cytotoxic activity and histological and immunohistochemical investigation. There are significant ascents in the level of ALP, SGPT and SGOT in case of liver disease in cancer. The ethanol extracts of combination of *Punicagrantum* L and *Ziziphus Mauritiana* (100mg/kg) remained the level of these parameters in the normal range. Total plasma proteins provide most convenient data in chronic liver diseases. Liver is the site of α, β globulins and albumin synthesis. Advanced liver diseases are characterised by decline in level of albumin and rising in level of globulin. Serum bilirubin is also exhibitive of hepatotoxicity. In the case of ethanol extracts of combination of both plants treated mice, the protein levels didn't alter significantly. The total bilirubin levels were also in normal range. In preliminary cytotoxic screening, considerable cell death was observed in the brine shrimp lethality bioassay particularly, ethanol extract of combination of both plants ZP (E) which showed promising activity. Brine shrimp lethality bioassay gave preliminary information about toxic nature of compound in rapidly multiplying cells and supported its cytotoxic nature. (Silva et al., 2007; Genupur et al., 2006). To confirm it's cytotoxic activity, study was further carried out in Ehrlich Ascites Carcinoma (EAC) cells. Ethanol extract of combination of *Punicagrantum*L and *Ziziphus mauritiana* caused significant cytotoxicity *in vitro* EAC cell. The results of the in-vitro cytotoxicity assay revealed that ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana* is toxic to the EAC cells as there was an increase in the number of cells stained with trypan blue dye, with an increase in the concentration of ZP (E). This cytotoxic activity might be due to mechanisms other than direct catalytic affects such as directly on the tumor cells and cause their lysis and/or indirectly by destroying the microenvironment i.e., the ascites fluid produced by the tumour cells (Berenbaum, 1970). In the present study, revealed that after treatment with ethanol extract of combination of both plants ZP (E), the caspase- 8 and 9 activity were increased and also histological study of stained EAC cells section from EAC bearing mice showed evidence of apoptosis such as shrinkage, plasma membrane blebbing, apoptotic bodies, fragmentation of nuclei and cytoplasmic azurophilic lytic vesicles. To prove this clarification based on morphologic, the mediator such as p53, Bcl-2 and TdT which involved in the molecular mechanism of apoptosis were detected by immunohistochemical methods. Presently, it well perceived that apoptosis is a form of cell death characterized by active suicide of cells. Hence, the study of this process is a profitable in cancer therapy (Sobenin et al., 1998) by elimination of seriously damaged cells or tumor cells by chemoperventive or chemotherapeutic agents (Galati et al., 2000; Thompson, 1995). The cells have undergone apoptosis which have frequently shown chromatin condensation and DNA fragmentation. They are immediately recognized by macrophages before cell lysis and then can be evacuated without inflammation. Hence, apoptosis inducing compounds are anticipated to be ideal anticancer drugs. Phenolic compound (phenolics acids, flavonoids, tannins) have been found to affect cancer cell growth by inducing apoptosis in many cell lines such as the hepatoma ($HepG_2$), the colon (SW620, HT-29, CaCo-2, and HCT-116), the prostate (DU-145 and LNCaP), the lung (A549), the breast (MCF-7), the melanoma (SK-MEL-28 and SK-MEL-1), the neuroblastoma (SH-SY5Y) and the HL-60 leukemia cells (Ramos et al., 2005; Ramos, 2007).Pervious phytochemical analysis have revealed presence of bioactive phenolic compounds in both plants (Agata et al., 2009; Sharrif and Hamed, 2012). Apoptosis relies on the balance between pro-apoptotic protein for example P21, P53, Bax, Bid, Back, etc., and anti-apoptotic protein such as Bcl-2, Bcl-xl and survivin. Change in ratio of proapoptotic protein/antiapoptotic protein stimulates apoptosis process, so increase in level of pro-apoptotic proteins or decrease in level of anti- apoptotic proteins which lead to initiate the apoptosis process. (Bhattacharyya et al., 2003; Chinni et al., 2001; Giannakakou et al., 2001; Ahmed et al., 2009). There are two distinct but interconnected pathways in the regulation of apoptosis process, viz., death receptor pathway (Extrinsic) and mitochondria–mediated pathway (Intrinsic). Caspase-8 is frequently related with the inception of the death receptor pathways which are independent to mitochondria pathways whereas caspase- 9 is associated in the intrinsic pathways (Chen and wang, 2002; Hengartner, 2000). Apoptosis can be induced through the activation of death receptors including: Fas, TNFα R, DR3, DR4 and DR5 by their ligands such as FasL, TNFα, APO-3L/TWEAK and APO-2L/TRAIL respectively. Activated caspase-8 can stimulate apoptosis via two parallel cascades. Firstly, it can directly cleave and activate caspase -3 which induce apoptosis. Secondly, it can cleave pro-apoptotic proteins such as P53 and translocate its fraction to mitochondria, releasing cytochrome-c which sequentially activates caspase- 9 and caspase- 3 and initiates apoptosis certainly (Fuchs and Steller, 2000). The key element of the intrinsic pathways is the releasing of cytochrome-c from

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mitochondria to cytosol. Cytochrome-c together with Apaf-1 can activate caspase-9 following the activation of caspase-3 that finally leads to apoptosis (Nijhawan et al., 1997). The proteolytic (caspases) enzymes mediate the cleavage of DNA into fragments (Seraste and Pulkki 2000; Denault and Salvesen 2002; Kasibhatla and Tseng 2003). A cell undergoing apoptosis would illustrate the following morphological changes: cell shrinkage, membrane blebbing, chromatin condensation and finally DNA fragmentation. DNA fragmentation assay showed that the ethanol extract of combination of both plants ZP (E) induced ladder-like DNA fragmentation which is characteristic of DNA damage. Most anticancer drugs of plant origin or synthetic have been known to cause DNA damage or suppress its replication, not necessarily killing the cells directly but promoting apoptosis. During apoptosis, a specific nuclease (now known as caspase-activated DNase or CAD and pre-existed in living cells as an inactive complex) breaks the genomic DNA between nucleosomes and generates DNA fragments. This ladder has been used extensively as a marker in studies on apoptotic cell death (Wyllie, 1980; Nagata, 2000). Consequently, based on the present data, the synergic anticancer activity of ethanol extract of *Punica grantum* L and *Ziziphus mauritiana* was verified, so it can be considered beneficial for cancer therapy and further medicinal investigation.

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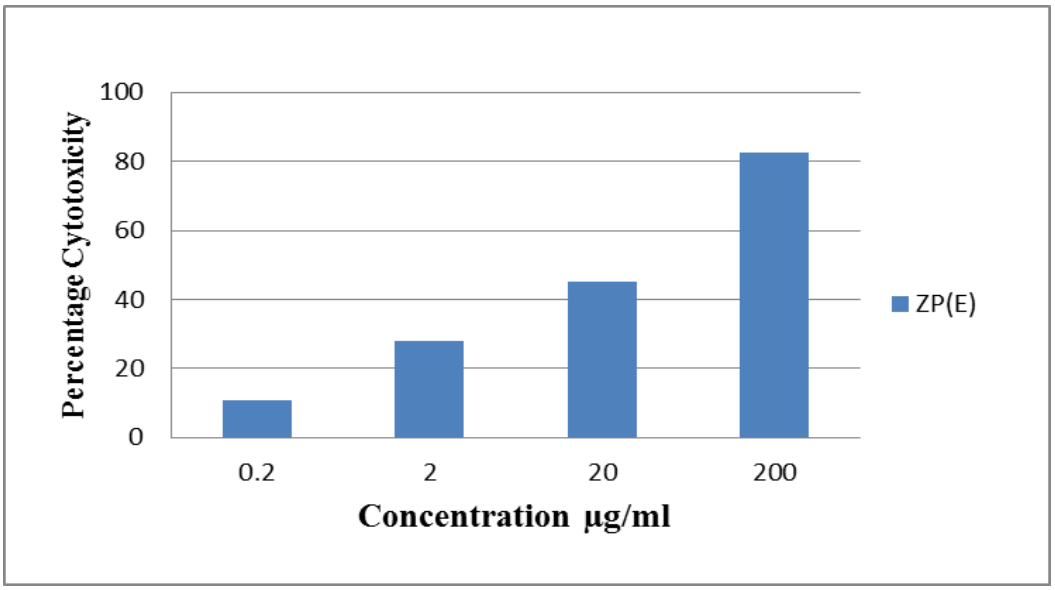


Figure 1: In vitro cytotoxic effect of ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana* on EAC cells. ZP (E): Ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana*

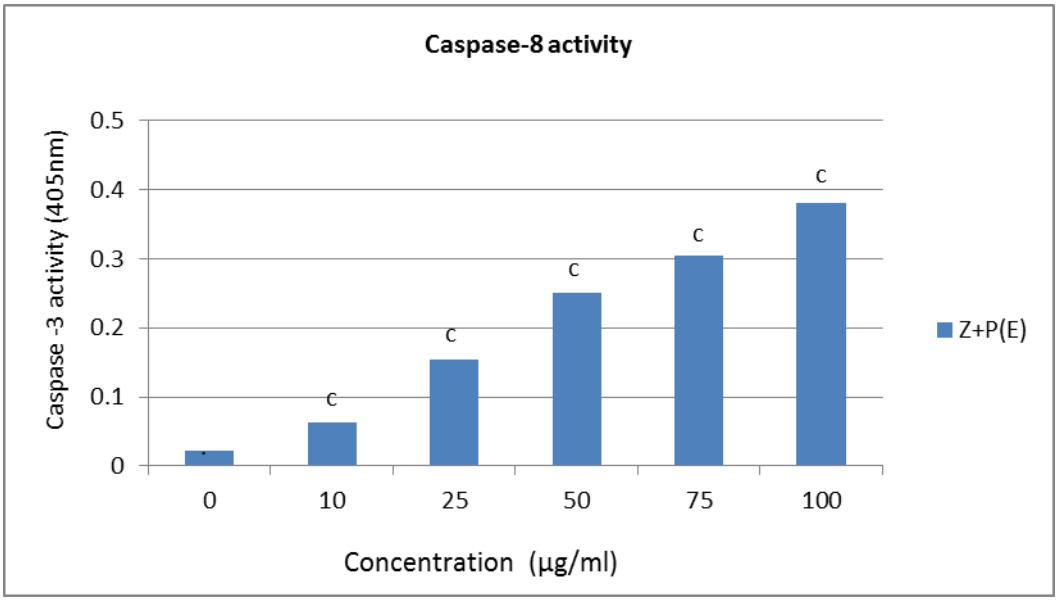


Figure 2: Caspase-8 activity of ethanol extract of combination of *Punica grantum* L and *Ziziphus maritiana*. n = 3, values are mean ± S.E.M, one way ANOVA followed by Dunnet's multiple test. P values: c < 0.001 as compared to untreated group as standard. Z+P (E): Ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana*.

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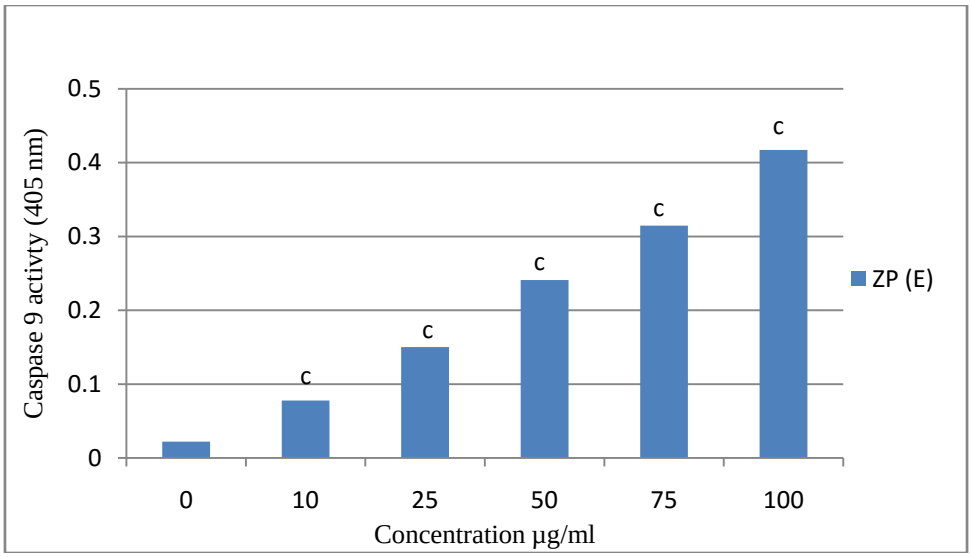


Figure 3: Caspase-9 activity of ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana.* n = 3, values are mean ± S.E.M, one way ANOVA followed by Dunnet's multiple test. P values: c < 0.001 as compared to untreated group as standard. ZP (E): Ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana.*

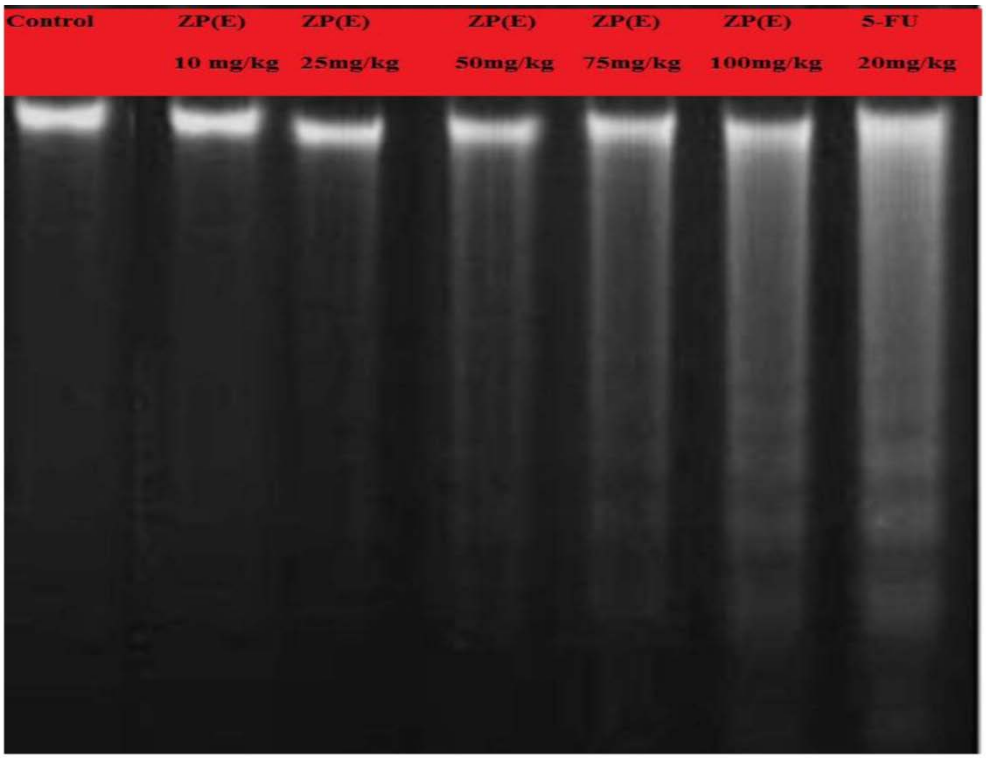


Figure 4: The ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana* developed DNA fragmentation in Ehrlich ascites carcinoma comparable to the effect of 5-Fluorouracil. 5-FU (5-Fluorouracil), Control (untreated EAC), ZP(E) (Ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana*).

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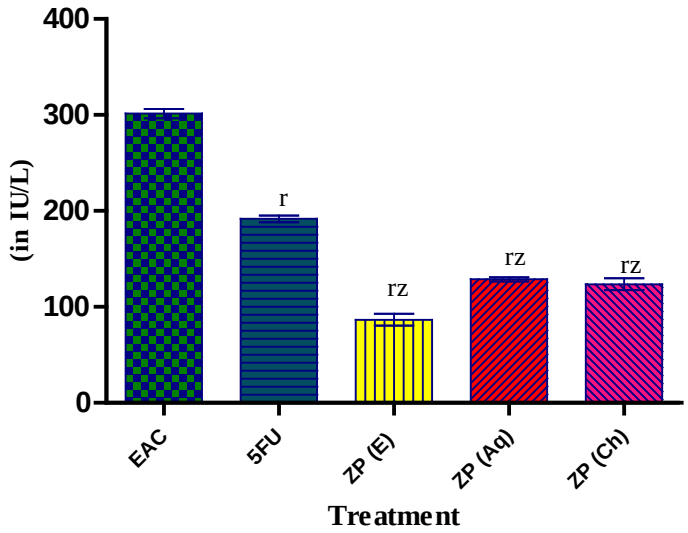


Figure 5: Effect of different extracts of combination of *Punica grantum* L and *Ziziphus mauritiana* on ALP level at dose of 100mg/kg, in EAC bearing mice. n = 6, Values are mean ±S.E.M, one way ANOVA followed by Dunnet's multiple comparison test. p values: r< 0.001, as compared with EAC control; z< 0.001, as compared with 5-Fluorouracil treated group. ZP (E): Ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana.* ZP (Aq): Aqueous extract of combination of *Punica grantum* L and *Ziziphus mauritiana.* ZP (Ch): Chloroform extract of combination of *Punica grantum* L and *Ziziphus mauritiana*.

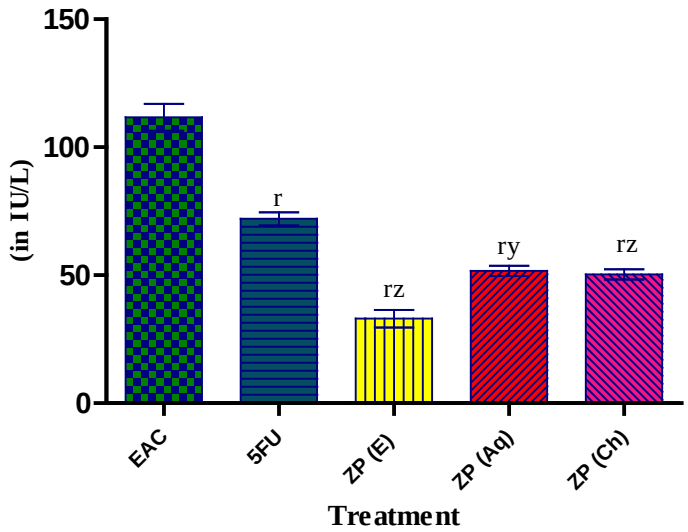


Figure 6: Effect of different extracts of combination of *Punica grantum* L and *Ziziphus mauritiana* on SGPT level at dose of 100mg/kg, in EAC bearing mice. n = 6, Values are mean ±S.E.M, one way ANOVA followed by Dunnet's multiple comparison test. p values: r< 0.001, as compared with EAC control; y<0.01, z< 0.001, as compared with 5-Fluorouracil treated group. ZP (E): Ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana.* ZP (Aq): Aqueous extract of combination of *Punica grantum* L and *Ziziphus mauritiana.* ZP (Ch): Chloroform extract of combination of *Punica grantum* L and *Ziziphus mauritiana*.

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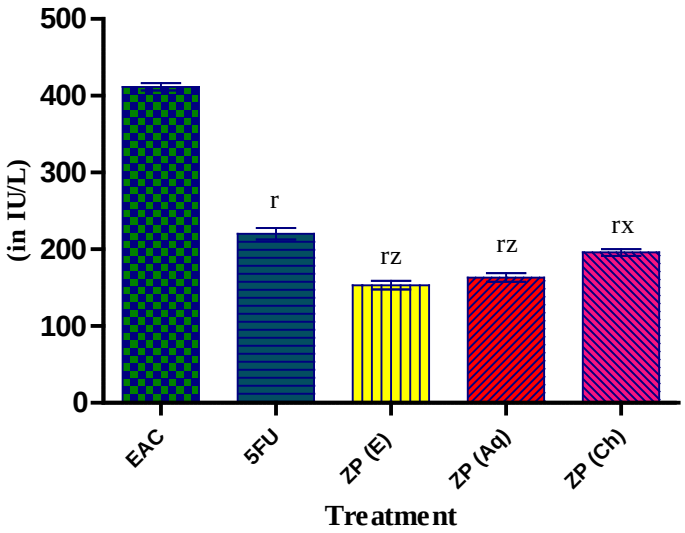


Figure 7: Effect of different extracts of combination of *Punica grantum* L and *Ziziphus mauritiana* on SGOT level at dose of 100mg/kg, in EAC bearing mice. n = 6, Values are mean ±S.E.M, one way ANOVA followed by Dunnet's multiple comparison test. p values: r< 0.001, as compared with EAC control; x<0.05, z< 0.001, as compared with 5-Fluorouracil treated group.ZP (E): Ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana.* ZP (Aq): Aqueous extract of combination of *Punica grantum* L and *Ziziphus mauritiana.* ZP (Ch): Chloroform extract of combination of *Punica grantum* L and *Ziziphus mauritiana*.

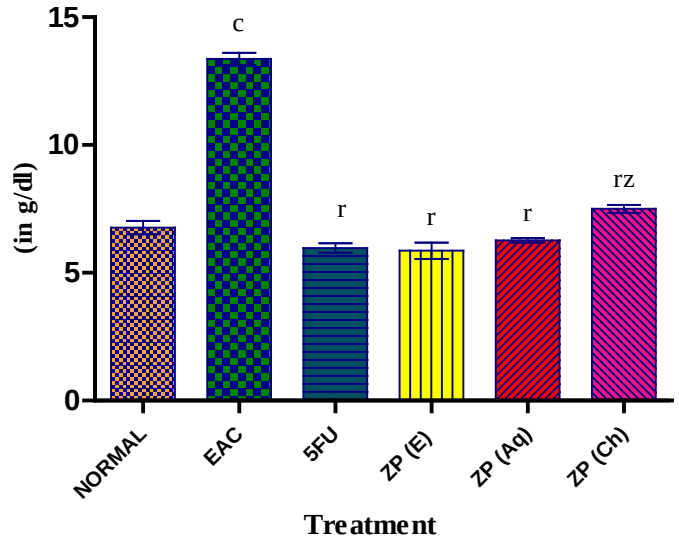


Figure 8: Effect of different extracts of combination of *Punica grantum* L and *Ziziphus mauritiana* on total protein content at dose of 100mg/kg, in EAC bearing mice. n = 6, Values are mean ±S.E.M, one way ANOVA followed by Dunnet's multiple comparison test. p values: c< 0.001, compared to the normal group; r< 0.001, as compared with EAC control; z< 0.001, as compared with 5-Fluorouracil treated group. ZP (E): Ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana.* ZP (Aq): Aqueous extract of combination of *Punica grantum* L and *Ziziphus mauritiana.* ZP (Ch): Chloroform extract of combination of *Punica grantum* L and *Ziziphus mauritiana*.

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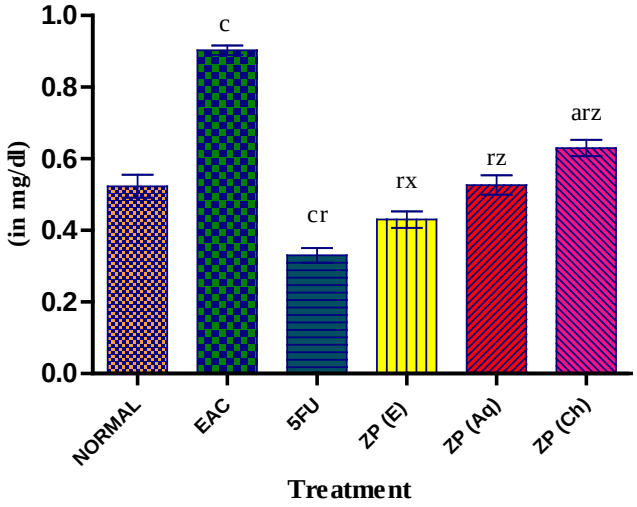


Figure 9: Effect of different extracts of combination of *Punica grantum* L and *Ziziphus mauritiana* on total bilirubin level at dose of 100mg/kg, in EAC bearing mice. n = 6, Values are mean ±S.E.M, one way ANOVA followed by Dunnet's multiple comparison test. p values: a< 0.05, c< 0.001, compared to the normal group; r< 0.001, as compared with EAC control; x< 0.05, z< 0.001, as compared with 5-Fluorouracil treated group. ZP (E): Ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana.* ZP (Aq): Aqueous extract of combination of *Punica grantum* L and *Ziziphus mauritiana.* ZP (Ch): Chloroform extract of combination of *Punica grantum* L and *Ziziphus mauritiana*.

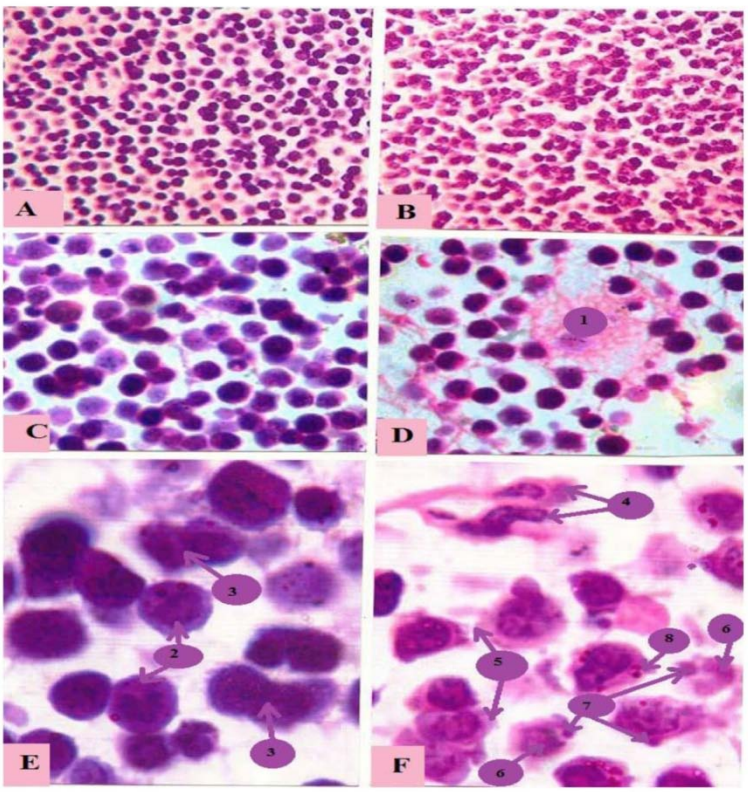


Figure 10: The picture of stained EAC cells sections depict decreased number of cells, necrotic area (1) (fig: 10D; × 400), irregular shrinked cells (4) (fig: 10B; × 100 and fig 10F; × 1000), plasma membrane blebbing (5), azurophilic eosinophilic vesicle (8), fragmenting nuclei (6) and apopoptic bodies (7) (fig 10F) by reason of remedy of EAC bearing mice with ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana* in comparison with EAC bearing control which indicated extremely proliferation and division of cells (3) with plentiful basophilic cytoplasm (2) (fig 10A; × 100, fig 10C; × 400 and fig 10E; × 1000).

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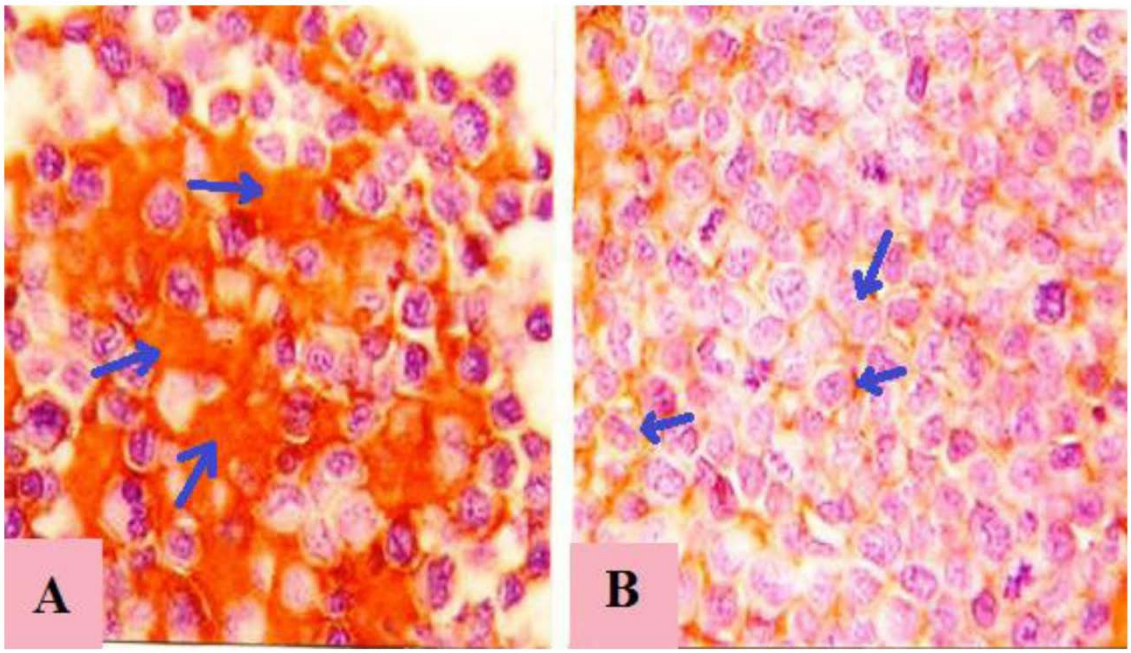


Figure 11: Immunohistochemically picture of stained EAC sections exhibited the higher concentration of Bcl-2 in the cytoplasm of EAC cells in untreated control mice (fig 11A; × 100) in comparison with ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana* treated mice. (fig 11B; × 100).

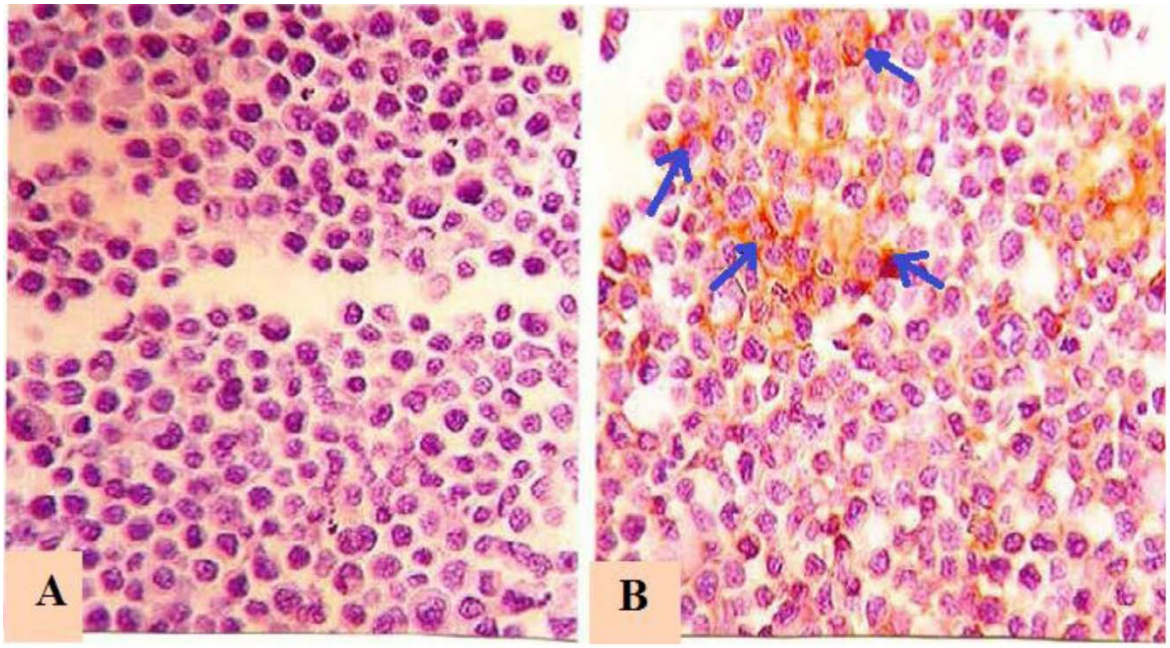


Figure 12: Immunohistochemically picture of stained EAC sections demonstrated the high concentration of p53 in the cytoplasm and nuclei of EAC bearing mice treated with ethanol extract of combination of *Punica grantum* L and *Ziziphus mauritiana*. (fig 12B; × 100) as compared with untreated control mice (fig 12A; × 100).

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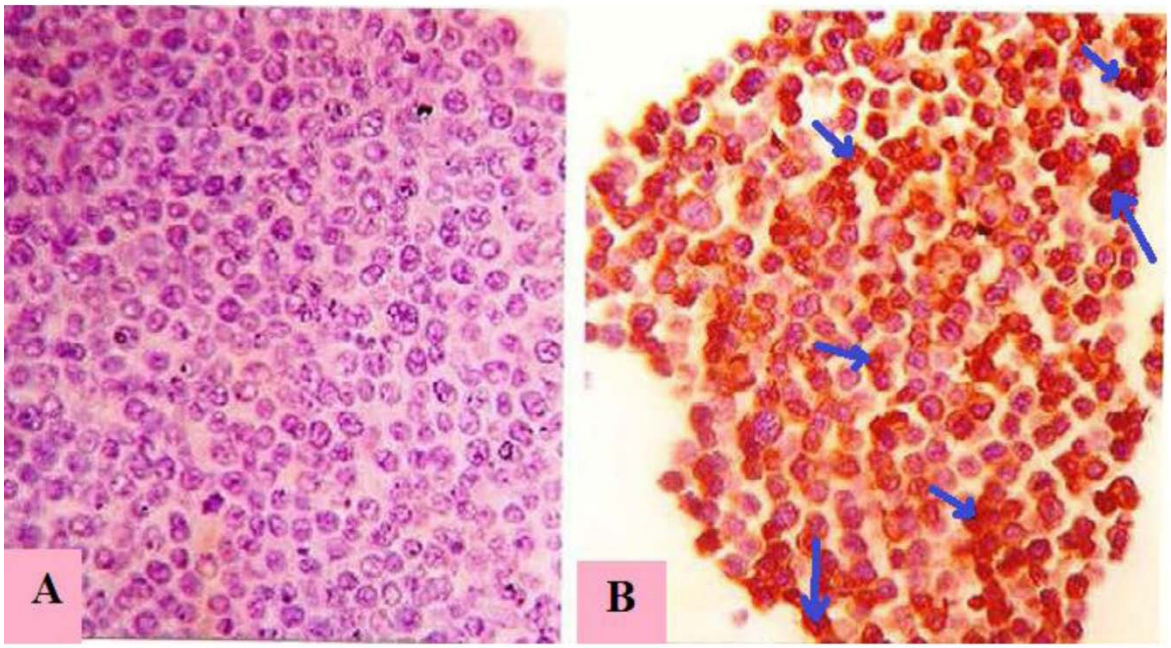


Figure 13: Immunohistochemically picture of stained EAC sections indicated the higher concentration of TdT in the nuclei of EAC cells bearing mice treated with ethanol extract of combination of *Punicagrantum* L and *Ziziphus mauritiana*.(fig 13B; × 100) as compared with untreated control mice (fig 13A; × 100).

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Assessment of Substance Abuse among Students of College of Health Sciences and Technology Ijero Ekiti

By Boluwaji Akinsefunmi, Ogboh Rita, Hassan Aminat & Babalola Rufus

College of Health Sciences and Technology

Introduction- Since the early times, medicinal plants have been used in healing and preventing diseases. The chronic use of substance(s) can cause some irreversible physical and psychological development[1]. The use of substance could be beneficial or harmful depending on how it is been used. Substance(s) could bring about a change in the biological function of living organism through its chemical composition[4]. It can also modify perception, cognition, mood, behaviour, and general body function[9]. They could thus be considered as chemical modifiers of the living tissues that could bring about psychological and behavioural changes[11]. The use and abuse of substance(s) by youths have become one of the most disturbing health related phenomena in society; several youths have become insane, irresponsible and liability to the society.

Substance(s) can be used for treatment or prevention of disease in man or animals; it also alters the body function, either positively or negatively, depending on the body composition of the user, type of substance(s) used, dose used, or combination with other substance(s) at the same time[3]. NAFDAC explains the term substance abuse as the excessive and persistent usage of a substance without regard to the medically or culturally accepted patterns.

GJMR-B Classification: NLMC Code: QV 600



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Assessment of Substance Abuse among Students of College of Health Sciences and Technology Ijero Ekiti

Boluwaji Akinsefunmi [α], Ogboh Rita [σ], Hassan Aminat [ρ] & Babalola Rufus [ω]

Chapter One

I. Introduction

Since the early times, medicinal plants have been used in healing and preventing diseases. The chronic use of substance(s) can cause some irreversible physical and psychological development[1]. The use of substance could be beneficial or harmful depending on how it is been used. Substance(s) could bring about a change in the biological function of living organism through its chemical composition[4]. It can also modify perception, cognition, mood, behaviour, and general body function[9]. They could thus be considered as chemical modifiers of the living tissues that could bring about psychological and behavioural changes[11]. The use and abuse of substance(s) by youths have become one of the most disturbing health related phenomena in society; several youths have become insane, irresponsible and liability to the society.

Substance(s) can be used for treatment or prevention of disease in man or animals; it also alters the body function, either positively or negatively, depending on the body composition of the user, type of substance(s) used, dose used, or combination with other substance(s) at the same time[3]. NAFDAC explains the term substance abuse as the excessive and persistent usage of a substance without regard to the medically or culturally accepted patterns. It could also be viewed as the use of substance(s) to the extent that it interferes with the health and social function of an individual[8]. In essence, substance abuse may be defined as the arbitrary over dependence or misuse of substance(s) with or without prior medical diagnosis from qualified health practitioners. Substance abuse can plainly be seen as the recurrent use of illegal substance(s) or misuse of the legal ones.

Substance abusers who exhibit symptoms of stress, anxiety, depression, behavioural changes, fatigue, and loss of appetite should be treated by medical experts and counsellors. Since the beginning of history, humans have searched for substances that would sustain and protect them and also act on the nervous system to produce pleasurable sensations[10]. Drugs are believed to provide pleasure because they give inner peace and satisfaction, relax the muscles and heighten sensation[2]. Students in Nigeria experiment with drugs without knowing which drug to take, when to take it and how to take it[7], and presently, risky alcohol use among students has become a serious public health issue in Nigeria [6].

The campus environment is free and young people often use substance to reassure themselves that they are able to express their freedom, some for the first time in their lives, which is a part of normal adolescent processes and perception of drugs as socially acceptable are all denominators of alcohol expectancy. Many adolescents use alcohol experimentally, sometimes frequently and sometimes consuming multiple drinks per occasion, without engaging in other problem behaviour's or experiencing immediate negative consequences[3]. It is a popular belief and equally a strong conviction among higher education students that the campus is a place of freedom and the perceived freedom ranges from academic to social, relationship, religious, and speech. The use of substance is most prominent in tertiary institutions where we have academic freedom and students do things at their own free will. Youths who are exposed to or who observe adults who drink and smoke may want to experiment to see how it feels[10]. If intervention is not quickly provided, this may signal the beginning of drug use and subsequently substance abuse and dependence.

A major factor in the use of substance by adolescents is concerned with sensation seeking and risk-taking tendencies and these tendencies are part of the normal developmental process for young people [10]. Youths or college students are in the stage of their lives where they experiment and look for new experiences, they want to try things out for themselves rather than relying on information provided by others. This sets them up to be vulnerable to the temptation to experiment with drugs/substance especially psychoactive ones. Many college students use legal drugs such as caffeine, nicotine or alcohol without much thought because their use is socially acceptable. The use of tobacco, alcohol, stimulants and other substances is a worldwide phenomenon. Youths get

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"high" from abusing substances such as inhalants, alcohol and cannabis among others[3].

The negative consequences of substance abuse on the well-being of Nigerian youths in all ramifications, has necessitated a clarion call for the Nigerian society to live up to it responsibility. Presently, youths vividly express high level of morally bankruptcy, decadent and helplessness detrimental to their growth and national development[1]. The Nigerian youths, considering the high level of competitiveness among nations of the world due to globalization are supposed to serve as the nexus of development and technological advancement. However, this expectation could be a mirage if the Nigerian youths with their challenge of drug abuse are not helped, re-orientated, revitalized and collectively salvaged together in order to prevent the total degeneration and loss of our societal values and ideals and a potential human capital developmental disaster. This is premised on the fact that the menace of substance abuse has eaten very deep into the fabrics of our society [5]. Majority of the Nigerian youths ignorantly without being aware of the consequences depend on one form of drug or the other for their various daily activities - social, educational, political, moral, etc. However, the consequences of substance abuse are so devastating and very shameful to the extent that both national and international organizations are also worried about the spread of this scourge among the Nigerian youths resulting to social violence among youths, armed robbery, mental disorders, 419 syndrome, social miscreants (Area boys and girls), school dropout, lawlessness, lack of respect for elders, rape, and many more of the social evils [9].

Therefore, the growing concern is that youths in Nigeria are highly involved in substance abuse at an alarming rate. For young people, substance abuse interferes with their cognitive and emotional development, increases the chance of accidental injury and death, and magnifies the likelihood of drug dependency. Substance abuse is a major gateway to crime and this undermine development by eroding social and human capital development. This degrades quality of life and has negative impact on the functioning and productive ability of youths [14].

This brings to bear the fact that though substance abuse is a major public health problem all over the world[11]. The use and abuse of substance have become one of the most disturbing health related phenomena in Nigeria and other parts of the world. It could also be viewed as the use of a drug to the extent that it interferes with the health and social function of an individual. Drug abuse is defined as the non-medical use of a drug that interferes with a healthy and productive life[13]. Drug abuse is the excessive, maladaptive or addictive use of drugs for non-medical purpose[12]. It can also be viewed as the unlawful overdose in the use of substance.

Majority of Nigerian youths ignorantly depend on one form of substance or the other for their various daily activities – social, educational, political, moral etc. Such drugs include: Tobacco, Indian hemp, cocaine, morphine, Heroine, Alcohol, ephedrine, Madras, Caffeine, Glue, Barbiturates, Amphetamines, etc.[6] in their studies on perception of Drug Abuse amongst Nigerian undergraduates identified dependence and addiction as one of the major consequence of drug abuse, characterized by compulsive drug craving seeking behaviours that persist even in the face of negative consequences. These changes are maladaptive and inappropriate to the social or environmental setting and could place the individual at risk of harm. In view of this context therefore, drug use among young people should be a matter of concern to all Nigerians, especially the government, parents, school heads, the leaders of religious groups and other NGO's[7].

a) Background of the Study

The consumption of substance(s) such as alcohol, amphetamine, cannabis, marijuana, caffeine, tobacco among others are now been taken frequently in large quantities by youths as they constitute the high risk of drug abusers. Today more youths are becoming drug dependent; those who are mainly from well-to-do homes are increasingly identified with the big boy[6].

The history of using mind-altering substance in excess, or in a manner disapproved by society, is as old as the human race. Fermented beverages were probably used by prehistoric humans, who depicted their effects on cave walls. Opium and marijuana have been in worldwide use for centuries and the Indians of South America recognized the stimulant properties of the coca plant long before the Spanish conquest. It is stated that all naturally occurring sedatives, narcotics, euphoriants, hallucinogens and excitants were discovered thousands of years back[8].

Each society develops rules and guidelines for the use of substance. Although the Bible frequently mentions wine in approving terms, it warns against drunkenness. In some cultures, men may drink fermented beverages to intoxication; women and children who do so may be punished. Alcohol use is widely accepted in western society, but its use is prohibited and condemned in Islamic cultures. In the eastern world, opium was once a widely accepted recreational drug. In the United State and England, it was available on grocery store shelves until the late nineteenth century Cocaine, the ingredient that was responsible about 100 years ago for making Coca-Cola "the pause that refreshes" is now an illegal drug in the United States. In the last decade or so, the growing rate of substance abuse has been causing a lot of concern in schools, government circles and the society at large. Substance abuse is not limited to any social and

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economic group neither is it limited to a particular sex or religion. Investigation into dimensions of this phenomenon has become necessary for it has become a cankerworm amongst youths especially students in many institutions in Nigeria.[19].

Drug is any chemical substance which when taken into a body organism modify one or more of its functions. In accordance with a definition substance such as alcohol, heroin and caffeine are drugs because these substances bring about modifications in behaviour by influencing co-ordination of the central Nervous System and sometime change the functions of the cell. Any chemical substances other than food that affects living organisms are drugs. Even common plants and animal preparations that are not pharmaceutical products but made for corrective purposes are drugs. To this group belong herbs, plants exudates latex, juice powder.[3]

The current trend of indiscipline among students and Nigerian youths in general has become so rampant that successive governments have sought for ways of combating its problems as a result of this unwholesome trend, school Boards, University Communities and Non-governmental Organization (NGOS) such as Youth Clubs, Philanthropic Organizations, Federal and State Governments and their parastatals, particularly the National Drug Law Enforcement Agency (NDLEA) have organized programmes to create awareness about the dangers of drugs and substance abuse[18].

Major-General Mohammed Buhari's regime (1983) for example, sought for adequate ways to eradicate social slogan popularly known as "War Against Indiscipline" (WAI). Some of the societal ills addresses were: [11]

- Disorderliness in public places
- Criminal activities like armed robbery, drug trafficking, and money laundering;
- Wanton destruction of public property and arson.
- Official corruption in all spheres of nation's life.
- Economic sabotage and graft by public officers, oil bunkering, currency trafficking, fraud, bribery and corruption (the main focus of the regime was to sanitize the polity and restore national values. General Ibrahim Babangida's regime (1985-1993) also tried to curb the influence of drugs which led to the promulgation of Degree IV and V of 1989 establishing the national Drug Law Enforcement Agency[11].

Similarly the Federal Ministry of Health (FMH) with the World Health Organization (WHO) later joined the International Council on Alcoholism and Addiction (ICAA) to curb drug addiction. Since then serious efforts have been made to conduct researches on the problems of drug abuse and the way of combating them by the NDLEA. This notwithstanding, alcohol, and cannabis still remain the most common substances of abuse in Africa. Existing literature on alcohol consumption among adolescents in sub-Saharan Africa suggests that a substantial proportion of adolescents have consumed or currently consume alcohol. Two studies conducted among students and among nationally representative samples of in and out of school youths found that the prevalence of lifetime alcohol use was approximately 25%. Substance misuse is a growing problem in Nigeria, as in many developing countries. Alcohol and cannabis are the most frequent substances of abuse[18].

The World Health Organization (WHO (2006) also defined drug abuse as a "state" of periodic or chronic intoxication, detrimental to the individual and to the society, produced by the repeated consumption of a drug (natural or synthetic). Drug abuse patterns include all aspect of drug usage by the youths ranging from how much, how often and what sort of drugs, where who, with, what circumstances and so on[18].

The analysis of contemporary social problem has consistently proved more and more controversial. There is a growing public concern in our country, Nigeria, about involvement of adolescents and young adult in drug abuse, which is defined as the non–medical use of substances by human beings that may modify one or more of its functions and may impair an individual ability to function effectively and may result in social physical or emotional harm. While it is universally accepted that drugs can be of tremendous benefit to man and society, it is also acknowledged that inappropriate use of drugs can be harmful to man .The personal, social and public health problems associated with psychoactive substance use, have continued to arouse worldwide interest and concern. Various reports and researches conducted have illustrated this phenomenon[15]. Drugs/substance abuse is a worldwide hazard with dangerous complications that affect many countries around the globe, Nigeria inclusive. The problem varies from place to place.

The African seminar on problems of drug dependence held in Lagos, Nigeria declared that "Drug abuse and dependence producing substances are widely prevalent in African countries have continue to increase. These problems affect the individual, the family and the society in general. Substance abuse which was originally conceived as the problem of a selected few is today becoming a problem of a sizeable proportion of the world population [17]. The problem is so grave that it has extended beyond the usual characteristic profile of abusers being male, adult, and urban-based to now include females, youngsters and those who live in rural areas. Its economic effect is so devastating that it is estimated that the annual retail cost of psychotropic substances by prescription is over two billion naira while the alcoholic industry which produces over five billion gallons of alcoholic beverages annually

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generate more than four billion naira from sales to a consumer population of about 30-35 million people[20]. Illicit Drug traffic known to generate huge profit and fortune and that is one reason why it has been very difficult to combat the drug traffic in spite of several laws that have been promulgated. For instance, it has been estimated that the sum of $400billion is the turnover of illicit drug industry, which is equivalent of approximately 8%of total international trade and therefore larger than the trade in iron steel, motor vehicle, textile, tourism[20].

Substance abuse and other associated problems constitute a major threat to the survival and effective functioning of human societies, lives are lost daily through addiction and activities of addicts. A significant number of deaths from accidents and violent crimes have been traced to the activities of persons under the influence of drugs. Treatment facilities nationwide are now gradually being over burden with drug-related problems and cases. The need to prevent drug abuse among the general population and by the growing generation of Nigeria thus becomes imperatives. Nigeria which once served only as trans-shipment route for drugs soon became a "consumer" country when it was observed that the increasing incidence of drug abuse among students is a contributory factor in the ugly confrontation between school administrators and students[12].

The problem of substance abuse poses a far greater health hazard than most imagine. Psychoactive drugs and substances have the primary effect on the mind such as altering mood, feelings, perceptions and behaviors. These drugs are usually taken to give insulation from the real world and its difficulties. This is accompanied by the feeling that varies according to the drugs used. This is common to those whose personality development is insufficient to enable them cope with the normal life[15]. One of the hazards of using of drugs/ substance to alter mood and feeling is that some individuals eventually develop dependent on the drug. They have diminished flexibility in terms of their behavior toward a particular drug or substance. They became dependent on the drug for their feeling well being. The intensity of this need or dependent may vary from mild desire to a craving or compulsion to use the drug/ substance and when the availability of the drug is uncertain they may exhibit a pre-occupation with its procurements[9]. In extreme form, their behavior exhibits the characteristics of a chronic relapsing disorder, this is a state referred to as "addiction or dependence". The substances commonly abused include tobacco, alcohol, stimulants like caffeine, nicotine, cannabinoids, amphetamine, volatile solvents like glue, petrol, diethyl ether, chloroform correction fluid, psychotropic medicines such as sedatives, anxiolytics, hypnotics etc. Most of the drugs being abused are beneficial, but also have devastating after effects such as psychosis, paranoid schizophrenia, and chronic addiction with all the implications of mental and physical dependency[13]. Some of the social and environmental contributory factors associated with substance/drug abuse include living away from home, relaxed parental control, alienation from family, early exposure to drugs, peer influence, easy access to the drugs and their availability etc.

b) Statement of Problem

The population of students in Nigeria's tertiary institutions has increased tremendously in recent time's .Statistical data shows that about one million five hundred thousand students are enrolled in more than 344 institutions in the country. Survey has revealed that Nigeria has about 63 Colleges of education, 50 polytechnics, 61 Monotechnics, 70 professional institutions which includes (school of Nursing, colleges of health technology, vocational institutes and the rest...) Figures in the last few years shows that Nigeria has over 100 universities altogether 33% accounts for the federal university while 44% accounts for the state university and 23% accounts for the private university[9].

The Nigerian youths constitutes (70%) of the entire population which is (124.95million) out of (178.5million) the general population and about (43%) of this population are affected with substance abuse and (28%) are students of various institutions.Globally, there were about 190 million substance abusers. Out of these substance abusers, around 40 million serious illnesses or injuries were identified each year; the trend is increasing as period goes. Recent trends indicate that the use of substances have dramatically increased particularly to claim the lives of 15 million people annually[6]. In recent years, the Federal government has approved billions of naira to drug enforcement agency (NDLEA) in collaboration with World Health Organization (W H O) to establish and maintain rehabilitation centres to cater for drug abusers that has been affected psychologically and has been mentally derailed[11].

Consequently, about 14% out of the 28% of the students that are involved in substances abuse usually becomes mentally derailed and they undergo rehabilitation and the remaining percentage of people exhibit deviant characters. Statistical analysis conducted by the W.H.O shows that a total of 15% deaths that can be traced to substance abuse are recorded annually 7% also accounted for youths[6].

Today, drug misuse and abuse is a major problem worldwide. Its extent and characteristics however vary from region to region although trends among the youths especially have begun to converge over these recent years. The most commonly used and abused substance is cannabis and alcohol. Alcohol and other related problems are becoming more a public health concern. The misuse of alcohol represents one of the leading causes of preventable death, illness and injury. Other common substances are inhalants, heroine

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and cocaine. This abuse is believed to be associated with increasing amounts consumed, frequency of use and groups involved[7].

The substance abuse problem in Nigeria is no different from other countries though there may be variations in the magnitude of the problem. It is difficult to say when it actually became a problem in Nigeria but its existence according to educated guesses could be traced as far back as the 1960s' after independence. Currently, use and abuse of drugs have expanded to include the youths[10]. This gives evidence that the people mostly affected are the young and strong who can contribute effectively to the economy of the country. Increasing youth's involvement in substance use and abuse is a major threat to national development, family stability and social security of the country.

To address these problems, various programs in Nigeria both official and unofficial have made several efforts towards curbing the menace of drug abuse (cigarette and hard drugs) of which the youths are the most gullible victims. Numbers of studies have also been carried out among in-school or out -of -school youths to gas their baseline information about the extent of the problem with respect to specific drugs such as tobacco. There is however the need to have information on the other commonly abused substances as well. This is because any sustained program that will bring interactions between the youths and their educators to allow opportunities for creating greater understanding of drug abuse and its social repercussions. Obviously a locally designed study aimed at vividly describing the extent of the problem on a broader scale looking at in school and out of school youths.[6]

Besides, the World Health Organization (WHO) through its Regional Strategy for Mental Health, aims at prevention and control of mental health and substance abuse disorders. It has a mandate to assist countries in assessing the magnitude of the problem to fill in gaps in knowledge, as well as develop epidemiological data for developing policies and prevention programs. The Nigeria Health Service has interest in taking advantage of this mandate so that the information generated through a youths' focused study could direct the design of evidenced-based prevention programs to address the problem[13].

Substance abuse is injurious to the students, it increases crime rates, enhances the spread of disease like AIDS, leads to loss of sanity, and death. Some students are involved in the use of illicit substance(s) because they want to reduce the peer pressure around them. Substance abuse among students in Nigeria in the contemporary time has become one issue that cast a gloomy shadow to the entire Nigerian society especially among students. Substance abuse and chemical dependency among young people has been a social problem and continues to be one of the most significant medical, social and economic problems facing mankind[22]. The prevalence of alcohol use on college campuses is classified as a "Major public health concern"[20]. The height of drug trafficking in Nigeria was witnessed in 1985 under the military regime. During this period, it was mostly the undergraduates that were caught and the first to be executed for drug offences under the "special tribunal (Miscellaneous Offences) Degree No. 20 of 1984. However, the abuse of substance is not only limited to the students as alien phenomenon is to distort its significance.

Nevertheless, the usage of substance either by students or other members of the larger society in all its ramifications appears to be a social problem. This problem is widely spread and it affect all and sundry. In other words, this wide spread use and abuse entice people from all walks of life and beyond the human destruction caused by drug dependence is the damage to traditional values and lifestyles. Studies have also shown that drug abuse wrecks individual, shatter families and weakens entire society with its burden of economic loses, health cost and increased lawlessness and crime. Also, substance abuse seems to undermine the ability of students to learn. Substance abuse also appears to contradict our values of physical wellbeing. To add to this, drug abuse may entail a lot of social problems ranging from lateness to lectures, family neglect, deviance behaviours, involvement in crime[16]. In terms of economic cost, it includes the more money required to deal with the undesirable effects of the drug abuse, the less money for services and programmes that enhances the quality of life[13].

Addressing the problem of substance abuse among adolescents in the college setting is a very specialized need with unique issues that demand "high quality and effective treatment" approaches that may be different to those used with other substance abuse populations or adolescents in general. Tertiary institutions as training institutions are different from secondary or high schools in structure, freedom, accountability, expectations and rules. As described earlier, campus environment is an adult world, with doors open to teenagers.

High rates of alcohol use are also associated with risky sexual behaviour among students. In a Nigerian study it reported that over 97,000 students are victims of alcohol-related sexual assault or alcohol abuse while several others reported being too intoxicated to know whether or not they consented to having sex[6]. The use and abuse of alcohol has implications on the health status of students in schools, for instance, it is the cause of many social and health problems, such as increase in crime rate and high proportion of accidental injury.

Many social, economic and political factors have contributed to the global spread of psychoactive substance. In the nineteenth century drugs tended to only be available where they were produced, or very

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close to the source of production. However, the growth of transportation, tourism and communications in the twentieth century has made it possible to transport goods and people quickly to any part of the world. Drugs too, are being transported to distant places. Given the economic rewards of producing and transporting drugs, it is not surprising that they are available almost all over the world. It has been estimated that the illegal market for drugs is worth $100 to $500 billion worldwide. These figures are of course more than estimates, but even at the lower level represent a substantial and lucrative market[7].

Global trends in drug production, transportation and consumption are difficult to describe and assess because of the complexities of the issues involved and the lack of accurate information on what are clandestine activities. Drugs are being produced in increasing numbers, making them more readily available through both legal and illicit channels. A drug culture life style with its own jargon support and maintains its members in their drug-seeking behaviour and helps to make the illicit market profitable. There has been a sizeable increase in the production and use of illicit drugs throughout the world. The United Nations International Drug Control Programmes estimate that the global production of coca leaf has more than doubled and that of opium poppies more than tripled since 1985[13]. Moreover, new forms of existing drugs e.g. smoke able "crack" cocaine, changes in the modes of administering these drugs e.g. transitions from opium smoking to heroin injection in South East, Asia and one introduction and proliferation of now synthetic drugs e.g. amphetamine-type stimulants and so called designer drugs all create new or exacerbate existing substances related problems. Of particular importance is the fact that drug injection has become a major transmission route for HIV of scientific and public health efforts to address these new issues, significant advances in drug abuse epidemiological research methods have been achieved. These advances have included improved techniques to assess the extent of drug related behaviours and problems, but also the introduction and development of methods which aim to understand behaviour as much as measure them. Substance abuse is a major social and public health problem. The abuse of one drug-alcohol-currently is one of the major causes of death in the United Sates, ranking only behind coronary diseases and cancer. Substance abuse cost the American economy billions of dollars a year[9].

To this end and judging from the problems outlined earlier, this research aims at assessing the level of substance abuse among students of College of Health Science and Technology Ijero Ekiti State.

c) Justification

The importance of this study is to provide resource materials for many that want to have deeper knowledge about the cause, effect and control of drug abuse. This research work will encourage organizations like NAFDAC, NDLEA, health organizations like WHO. and government parastatals to establish drug rehabilitation center to help victims of drug abuse more so the significant of this study is to outline its health implication amongst students which will be centered on identifying the cause of drug abuse among student, reducing the hazard of drug abuse to a minimum level, reducing the incidence of rape among students, and also to alert the government on how to control the abuse of drug since the sort term and long term effect are disastrous.

Recent studies show that the rate of juvenile delinquencies in Nigeria has drastically increased due to the indiscriminate use of drug among youths of Nigeria. Crimes such as Armed robbery, rape, theft, political thuggery, homeless children, drop out, killings e.t.c.[6]

While the use of tobacco by the general population has decreased over the last several decades, students' use of tobacco remains widespread[9]. The menace of drug use is not limited to Nigeria. The World Drug Report (2005) states that five percent of the world's population, aged 15-64, had abused drugs at least once in 2003. Some crimes committed under the influence of substances include murder, rape, robbery, homicide, destruction of lives and properties, violation of traffic regulations leading to accidents, affecting the user and or the people of the society in general.

The problem of drug abuse among youths in Nigeria has a unique slant because Nigerian tertiary institutions admit students who are still in mid-adolescence. The minimum age of entry into Nigerian institution is 16 years[33], which lowers the average age of students in tertiary institutions. Misconduct either appears or escalates in adolescence. Rates of substance use are higher in adolescence than during childhood[22]. This is possibly due to the fact that in the second decade of life, young people encounter a rapidly widening world of opportunity, accompanied by rapid changes in all areas of their lives.

This rapid growth or change occurs in various areas such as physical changes (development of secondary sexual characteristics of pubic hair, weight gain, deepening of the voice, fullness of the breast, etc), cognitive development (the movement from concrete to abstract thought processes.), and psychosocial development (identity formation and accompanying dilemmas in the struggle for independence on the way to adulthood). The widening world and rapid changes expose adolescents to serious risks before they have adequate information, skills and experience to avoid or counteract them[19]. One of such risks is the exposure to substance abuse which becomes one of the factors that influences the development of the burden of disease. The World Health Organization (WHO) also reported that

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one third of the disease burdens of adults can be associated with behaviors' that began in adolescence. It is on this background that researchers set out to establish prevalence of substance abuse among students in tertiary Schools. This particular research work will attempt to assess the level of substance abuse, and the research findings may contribute towards providing information assessing the level of substance abuse among youths. The problem of drug abuse being of public health importance needs to be effectively and efficiently control, to greatly reduce the menace and consequences such as crimes and cultism. College of Health Science and Technology is highly cosmopolitan with students admitted from all over Nigeria. It has been in one forefront in the training of high and middle level manpower for the health sector of the nation's economy, therefore the project will have a great impact on many youths and the nation in general[2].

d) Objective of the Study

i. *Main Objectives*

The main objective of this study is to assess the level of substance abuse among the students of College of Health Sciences and Technology.

ii. *Specific Objectives*

1) To assess the knowledge and source of substance abuse.
2) To determine the substance commonly abused among students.
3) To determine the level of substance abuse.
4) To assess the consequences of substance abuse among students.

e) Scope of the Study

The study was conducted among students of College of Health Science and Technology in Ijero Ekiti

f) Significance of the Study

The need to assess the level of substance abuse among College of health student in Ijero Ekiti is to;

1. Know the level of dependency, tolerance, and addiction of abused substance.
2. Highlight the risk and consequences of substance abuse.
3. The data collected will help to know the frequency or level of substance abuse among students.
4. To help reduce the hazard of drug abuse among students

This study will provide resource materials for many that want to have deeper knowledge about the causes, risk, consequences and level of substance abuse among students.

Chapter Two

II. Literature Review

a) Overview of Substance Abuse

Drugs are generally defined as substances other than food, which are taken to change the way the body or the mind functions. These drugs could come from plants growing wild in the fields or they could be manufactured in the laboratory. They could also be categorized into legal, illegal, or harmful. These drugs are considered abused when the user deliberately uses it for non-medical purposes, as well as the arbitrary use without Medical prescription.

Drug or substance abuse comes in various shades. This involves taking too much of a drug at one time or small doses at shorter intervals. Taking a drug at regular intervals but far beyond the duration given or taking it for a wrong reason is also abuse. A drug again can be abused if it is taken in combinations with other drugs knowingly or unknowingly.

More often users move from one drug to another and use combinations of different substances. Some of these combinations could be so dangerous to cause sudden death. Drug refers to a substance that could bring about a change in the biological function through its chemical actions[7]. It is also considered as a substance that modifies perceptions, cognition, mood, behavior and general body functions[5]. This could thus be considered as chemical modifiers of the living tissues that could bring about psychological and behavioral changes[5].

Drug abuse is a major public health problem all over the world[9]. The use and abuse of drugs by adolescents have become one of the most disturbing health related phenomena in Nigeria and other parts of the world. Several school going adolescents experience mental health problem, either temporarily or for a long period of time. Some become insane, maladjusted to school situations and eventually drop out of school[9]. The term drug abuse was defined as excessive and persistent self-administration of a drug without regard to the medically or culturally accepted patterns[4].

It could also be viewed as the use of a drug to the extent that it interferes with the health and social function of an individual. Drug abusers who exhibit symptoms of stress, anxiety, depression, behavior changes, fatigue and loss or increase in appetite should be treated by medical experts and counselors to save them from deadly diseases[10].

The alarming evidence in the prevalence of drug abuse, the effects and consequences of substance abuse among students has called for concern and challenge to all helping professions to mount strategies of equipping youths with skills of living devoid of substance abuse.

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In Nigeria today, the consequences of substance use are diverse, including acute and chronic health, social as well as psychological problem. There is disruption of interpersonal relationships particularly within the family, marginalization, criminal behaviour, school failure, vocational problems and failure to achieve normal adolescent milestones, yet these adolescents are expected to be the leaders of the country in the future when they do not even have any focus for the future. Several studies carried out among the secondary school students in Benin City found out that students and youth of easy virtue in the community are involved in cannabis abuse and stimulants such as amphetamines and cannabis[13]. The consensus of opinion therefore seems to be that youths are also seriously involved in substance abuse.

Drug abuse has become such a problem of great concern to all well-meaning Nigerian and particularly the Federal Government to the extent that an Agency has been established to combat the social disease with a view to reducing the spread of drug abuse to the barest minimum or eradicating it totally.

People abuse drugs for various reasons. These may range from curiosity, availability and previous drug use to emotional and social pressures. Drug use and abuse as a habit unfortunately could begin quite early in life as part of culture in some societies. The common drugs that are abused and which have attracted both local and international concern include tobacco, marijuana, heroin, cocaine, valium and ecstasy. According to World Health Report (1995), levels of use of marijuana and other illicit substances among the young people in the USA since 1992 have increased for the first in over ten years. Lifetime use of any illicit drug among 18 year olds in school peaked in 1981 at 66%. It again states that drug injecting is increasingly becoming common. Often, injecting implies sharing needles with its resultant risk of HIV infection, hepatitis among other infections. A crude estimate of mortality worldwide due to drug injecting is between 160,000 and 210,000 per year[4].

Volatile solvents and inhalants are presently common among younger and marginalized people in developing and developed countries.

Internationally, there have been several meetings to deliberate on the menace of drug abuse. For example in 1990, Mr. Perez de Cueller, at the special session of the United Nations indicated that drug abuse is a time-bomb ticking away in the heart of civilization and there was the need to quickly find measures to deal with it before it explodes and destroys. In a similar meeting in 1998, Ghana's Mr. Kofi Annan, United Nations Secretary-General, also stated that "the proliferation of drugs over the past 30 years is an example of the previously unimaginable, becoming reality very quickly and a tragic reality that historians will record as the time when the international community has found a common ground in a mission to increase momentum towards a drug free world in the 21st century".

Nigeria has over the years made positive strides in curbing the drug menace among its populace. Efforts have included the development of policies against drug trafficking through national and internal ports of entry, confiscation of property of drug traffickers, banning of cigarette advertising on television, banning of smoking in public places, institution of annual drug awareness campaigns in collaboration with international partners such as WHO and the inscription of the surgeons warning on the danger of smoking on each cigarette packet.

A number of studies have been carried out in Nigeria and other parts of Africa to look at the prevalence of selected drugs such as tobacco among the youth. In a study by WHO, results indicated that, out of a total of100respondents, 14% had ever smoked cigarette, 19% currently use a form of tobacco. It was reported that 15.1% of respondents had been offered free cigarettes by tobacco company representatives before. About 55.9% had been taught in class in the past year about dangers of smoking.

In another study by same author on tobacco involving 510 tertiary institutions students in 6 schools, 65 (13%) had ever smoked cigarettes. Of these 13%, 15(23%) started at the age of 16. 26% of the total sample were aware that smoking caused harm to the lungs. This habit is as a result of peer pressure, parental smoking and advertising.

Due to paucity of information on the drug problem and limited resources, few studies if any have been able to investigate the prevalence of abuse over a wide range of commonly abused substances within the Nigerian setting.

Substance abuse is a social problem that has spread and increased rapidly in our educational institutions especially among our secondary school students. In Nigeria, this social mal adaptation is considered an issue of serious concern as it adversely affects the lives and performance of students involved as well as the harmonious functioning of the entire structure of the society. Drug abuse and other associated problems are inimical to the survival and effective functioning of human societies. A significant number of untimely deaths and accidents have been ascribed to the activities of persons under the influence of one drug or the other.

Substance abuse is the use of mood modifying substances illegally, excessively and in a socially unacceptable manner[13]. The drugs range from those that should not even be taken without medical prescription such as cocaine, amphetamine, heroin, marijuana, to the socially acceptable beverages such as whisky, local gin, beer and other alcoholic drinks. It was viewed that substance abuse is the improper use or

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application of drugs by a person without proper knowledge of the drugs and without due prescription from a qualified medical practitioner[15].

b) Theories of Substance Abuse

Theories of drug abuse indicate that some people truly depend on certain drugs for their survival due to a number of factors. The major emphasis of the theories is that people have their individual reasons for depending on one type of the drug or the other. Such reasons are explained by the following theories. Personality theory of drug abuse, learning theory of drug abuse, biological theory of drug abuse and socio-cultural theories[15.]

Personality Theories of Drug Abuse: The main emphasis of the theories are that there are certain traits or characteristics in the individuals that abuse drugs. Such personality characteristics, are inability to delay gratification, low tolerance for frustration, poor impulse control, high emotional dependence on other people, poor coping ability and low self-esteem. Individuals with these personality characteristics find it difficult to abstain from drug abuse.

Learning Theory of Drug Abuse: It maintains that dependence or abuse of drugs occurs as a result of learning. The learning could be by means of conditioning, instrumental learning or social learning.

Biological Theory of Drug Abuse: The theory maintains that drug abuse is determined by the individual's biological or genetic factors which make them vulnerable to drug addiction

Socio-cultural Theories of Drug Dependence/Abuse: The theories maintain that abuse is determined by socio-cultural values of the people. For instance, while certain cultures permit the consumption of alcohol and marijuana, other cultures do not. Among the Urhobo, Ijaw, Ibibio, Edo, Igbo, Yoruba and Itesekiri, alcohol i.e. Ogogoro is used in cultural activities. In Northern Nigeria, alcohol is forbidden due to Sharia law.

However, the sharia law does not forbid cigarette consumption and thus nicotine dependence. It should be noted, however that no theory fully explains the etiology of drug abuse. This is due to individual differences. It then becomes obvious that the disorder (drug abuse) is an acquired one. The acquisition then is dependent on a host of personal inclinations and environmental factors, social cognitive theory, i.e the triadic reciprocity involving behavior, environment and the person.This definition focuses on psychoactive drugs; all drugs can be abused to an extent that it turns into addition when the drug user is unable to stop the use of drugs despite the harmful effects on the user's social, personal and economic lives.

The problem of substance abuse is so grave that though it was originally conceived as the problem of a 'select few', it has extended beyond the usual characteristics of abusers being male, adult and urban based people to now include female, youngsters and rural dwellers. These abusers erroneously believe that drugs enhance their performance, put them in good mood, the accompany problems of this act constitute a major threat to the well-being of the society[22].

The youths in Nigeria like many countries of the world are developing addiction to psychoactive substances. In 1992, the National Drug Law Enforcement Agency (NDLEA) collected drugs use and abuse data from schools, records of patients admitted at mental health institutions for drug problems and interview of persons arrested for drug offences. The result showed that youths constitute the high risk group for drug trafficking and abuse. Friends and school mates account for about 90% of the source of influence of the use and abuse of various psychoactive substances. In Nigeria, alcohol and cigarette are legal substances but, the two have been discovered to cause physical damage to human bodies. These substances have also said to be "gateway drugs" to other more potent drugs like heroin and cocaine[6]. In Nigeria, it has been reported that smoking (tobacco) causes 90.0% of lung cancer, 30.0% of all cancers, and 80.0% of other chronic lung diseases[17]. There is a strong need for such a study to be carried out among in school and out of school youth to determine the prevalence and social consequences of substance abuse among them.

c) Sources of Substance(S) Commonly Abused Among Students

A Nationwide survey on drug use among students found that the large majority of pupils (85.6%) considered themselves to be sufficiently informed about drugs, their effects and the problems associated with their use (Morales et al, 2008). The main channels through which young people received drug use information were their parents and siblings (73.2%), the media (69.3%) and teachers (63.8%). Nowadays there is a considerable increase in number of student gaining drug information and knowledge via their families and teachers. In this regard, students will have received sufficient drug information by the time they leave secondary school[19]. In 2003, 60% of school pupils received information on drug use in the context of health educational classes; this figure had reached 100% by 2008. It is therefore prudent that school become the resource and center where drug information is accessed.

The factors associated with drug abuse are many and varied, and include individual predispositions, family characteristics and complex social and environmental determinants.

A number of authors and researchers have shown that there are many contributing factors to drug abuse among students. It was stated that in a school

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setting, drug abuse affects the children of the rich as well as those from poor families [20].

Drug abuse is caused by a combination of environmental, biological, and psychological factors. Under environmental factors; the most influential elements include the family, peer association, school performance and social class membership.

According to the United Nations (1992), drug users, like approval for their behavior from their peers and using is a symbolic to the group. Whether peer pressure has a positive or negative impact depends on the quality of the peer group. Unfortunately, the same peer pressure that acts to keep a group within an accepted code of behavior can also push a susceptible individual down the wrong path.

A study carried out in Nairobi secondary schools indicated that the majority of drug users had friends who used drugs[16]. Studies on the issue of drug use and abuse agrees that there is a significant relationship between the subjects‟ drug using behavior and the involvement of their friends in drugs[15]. According to the study, if an adolescent associates with other adolescents who use drugs, the risk of involvement with drugs is further increased. Another survey of youths in southern Nigeria, also found out that the source of drugs for drug using-students was friends in the same or neighboring schools, and students who reported using drugs had more drug using friends than abstinent friends[7]. Confirming this finding, it was argued that peer pressure influences youth to use substances under the false impression that some drugs stimulate appetite for food, increase strength and give wisdom as well as courage to face life[16].

Although it is presumed that there are similarities in the prevalence of psychoactive substance use, authors has asserted that there are various factors that cause young people to abuse drugs and even become addicted. These include family networks, interaction and home environments[18].

It was reported that adolescents with substance abusing parents experience a higher rate of parental and or family problems than do adolescents whose parents do not abuse substances. This may cause poor parent-child attachment, which may in turn lead to a lack of commitment to conventional activities, thereby at times leading to adolescent drug taking[14]. It was added that youths with poor home support tend to seek support and understanding elsewhere. Many find affection, understanding and support in the lifestyle of a drug abusing subgroup[20].

It was added that interactions within the family unit will play a major role in the adolescent's personality or self-concept formation. In addition, the exposure to cultural norms through the family, as well as individual adaptations, lays the foundation for influential modelling and acceptance of social orientations. The family is often viewed as the basic source of strength, nurturing and supporting its members, as well as ensuring stability and generational continuity for the community and its culture[15].

d) Causes of Substance Abuse among Students

The followings are the main causes'

1. *Experimental Curiosity:* Curiosity to experiment the unknown facts about drugs thus motivates adolescents into drug use. The first experience in drug abuse produces a state of arousal such as happiness and pleasure which in turn motivate them to continue.
2. *Peer Group Influence:* Peer pressure plays a major role in influencing many adolescents into drug abuse. This is because peer pressure is a fact of teenage and youth life. As they try to depend less on parents, they show more dependency on their friends. In Nigeria, as other parts of the world, one may not enjoy the company of others unless he conforms to their norms.
3. *Lack of parental supervision:* Many parents have no time to supervise their sons and daughters. Some parents have little or no interaction with family members, while others put pressure on their children to pass exams or perform better in their studies. These phenomena initialize and increases drug abuse.
4. *Personality Problems due to socio-Economic Conditions:* Adolescents with personality problems arising from social conditions have been found to abuse drugs. The social and economic status of most Nigerians is below average. Poverty is widespread, broken homes and unemployment is on the increase, therefore our youths roam the streets looking for employment or resort to begging. These situations have been aggravated by lack of skills, opportunities for training and re-training and lack of committed action to promote job creation by private and community entrepreneurs. Frustration arising from these problems lead to recourse in drug abuse for temporarily removing the tension and problems arising from it.
5. *The Need for Energy to Work for Long Hours:* The increasing economic deterioration that leads to poverty and disempowerment of the people has driven many parents to send their children out in search of a means of earning something for contribution to family income. These children engage in hawking, bus conducting, head loading, scavenging, serving in food canteens etc and are prone to drug taking so as to gain more energy to work for long hours.
6. *Availability of the Drugs:* In many countries, drugs have dropped in prices as supplies have increased.

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7. *The Need to prevent the Occurrence of Withdrawal symptoms:* If a drug is stopped, the user experiences what is termed "withdrawal symptoms". Pain, anxiety, excessive sweating and shaking characterize such symptoms. The inability of the drug user to tolerate the symptoms motivates him to continue[21].

Drugs are abused for various reasons: It was confirmed that search for pleasure motivates drug abusers to alter their state of consciousness. The studies confirmed that people abuse drugs for the enhancement of good feelings and used it as a means of coping with stress of life[17].

Advanced reasons for substance abuse in Nigeria: Intra-individual reasons, Sex, Physical or mental illness, Personality make up, Extra individual reasons, Dependence producing nature of the drugs and Availability[18].

Intra-individual reasons pertained to the individuals and these include age, sex, physical and mental illness. Studies have shown that young people especially adolescents and young adults are most prone to drug abuse.

A survey carried out by National Drug Law Enforcement Agency (NDLEA) revealed that they abuse drugs as early as age eleven (for prescribed drugs) and age 16 (for narcotic drugs). The reasons advanced by these students are: to feel on top like adults, to feel good, to get excited, to be like friends and to be like stars. Drug abuse is sex based, more males than females abused drugs[19]. However it was stated that there are as many males as there are females who abuse drugs. Individuals with physical or mental illness are more likely to use drug than those without such illness. These individuals are more pre-disposed to over use of or over dependence on drugs to control and treat such ailments[24]. The use of these drugs outside medical prescription constitutes drug abuse.

Individuals differ in their makeup and in the way they respond to situations and events in their environment. The ability to tolerate or yield to stress, frustrations, pain and discomfort determines whether an individual will become a drug abuser or not. It could be inferred that drug abusers are usually weak and unable to cope with stress, pain or discomfort. Thus, drugs foster a sense of relaxation and sedation which help abusers to escape the reality of environmental stress, such as urbanization, the pressure to get ahead in school and business, unfair distribution of income, poverty and family problems.

There are external reasons that act on the individuals. Drug abusers usually described such factors as those of peer pressure, the urge to be curious and wish to experiment, unemployment, idleness, unstable family conditions, for example, death, separation, boredom, poverty, affluence and the bustles of city life. Extra individual reasons include the need to get rich quickly (drug trafficking), to enhance performance (especially among the athletes and artists) and drug use in the family (NDLEA, 1991).

Dependence producing natures of the drugs are reasons which have to do with the drugs. A drug continually used for a period produces dependence, thus making it difficult for the user to quit the tranquil sedatives and analgesics are the most common dependence producing drugs.

Drugs that are readily available such as alcohol and tobacco can be easily abused. In 1991, more than 12% of the students in Lagos State indicated that it was easy to get illegal drugs like cannabis, heroine, and cocaine. About forty percent (40%), indicated that these drugs could be gotten, though with a little difficulty (NDLEA, 1991). Researchers have clearly shown that all the reasons stated above curiosity and experimentation are the most valid for young people[21].

e) Signs and Symptoms of Substance Abuse

According to Adolescents Health Information Project AHIP (2001) the following are signs and symptoms of drug abuse. They are:

A. Signs of Drug Used and Drug Paraphernalia

i. Possession of drug related paraphernalia such as pipes, rolling paper, small decongestant
ii. Possession of drugs, peculiar plants or bolts, seeds of leaves in ashtrays or clothing pockets.
iii. Odour of drugs, smell of incense or other cover up scents.

B. Identification with Drug Culture

i. Drug related magazines, slogans on clothing
ii. Hostility in discussing drugs

C. Signs of Physical Deterioration

i. Memory lapses, short attention span, difficulty in concentration.
ii. Poor physical coordination, slurred or incoherent speech; unhealthy appearance, indifference to hygiene and grooming
iii. Bloodshot eyes, dilated pupils.

D. Changes in Behavior

i. Distinct downward performance in school place of work.
ii. Increased absenteeism or tardiness.
iii. Chronic dishonesty, lying; cheating and stealing.
iv. Trouble with the police and other law enforcement agencies
v. Change of friends, evasiveness in talking about new ones.
vi. Increasing and inappropriate anger, hostility, irritability etc.
vii. Reduce motivation, energy, self-discipline, self-esteem etc.

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f) Types of Substance Commonly Abused

In Nigeria, the most common types of abused drugs according to NAFDAC (2000) are categorized as follows:-

1. *Stimulants:* These are substances that directly act and stimulate the central nervous system.

   Users at the initial stage experience pleasant effects such as energy increase. The major source of these comes from caffeine substance.
2. *Hallucinogens':* These are drugs that alter the sensory processing unit in the brain. Thus, producing distorted perception, feeling of anxiety and euphoria, sadness and inner joy, they normally come from marijuana, LSD etc.
3. *Narcotics:* These drugs relive pains, induce sleeping and they are addictive. They are found in heroin, codeine, opium etc.
4. *Sedatives:* These drugs are among the most widely used and abused. This is largely due to the belief that they relieve stress and anxiety, and some of them induce sleep, ease tension, cause relaxation or help users to forget their problems. They are sourced from valium, alcohol, promethazine, chloroform.
5. *Miscellaneous:* This is a group of volatile solvents or inhalants that provide euphoria, emotional disinhibition and perpetual distortion of thought to the user. The main sources are glues, spot removers, tube repair, perfumes, chemicals etc.
6. *Tranquilizers:* They are believed to produce calmness without bringing drowsiness; they are chiefly derived from Librium, Valium etc.

Other substances commonly abuse includes

-Alcohol
-Cigarette
-Cannabis
-Cocaine
-Tranquilizer
-Heroin

The local names for these drugs were given as follows:

Alcohol: Akpeteshie/ Akpet, Apio, Kasapreko, Palmwine, VC10, Bonsamnsuo (satan's water) Gin, Yebudidi (for appetite), Abreman, Power, Damn Booze, Gordon Spark, Juice, Bonsamdwonso (satan's urine) Kwaff, Pure water, and APC, pito, brandy, satan's urine, castle milk stout (CMS), Guinness, spirit (black and red label, schnapps), Africa, Saviour, trigger, star, beer, castle milk stout. Means of Administration is by drinking.

Cigarette /Tobacco: Embassy, Diplomat, Jot, 555, Cigar, Tobacco, Foo, Owoakasee (death bone), Pipe, Stroke, Taaba, Nwisie (smoke), Stick, Royals, Bonds, Nsatea (long fingers), Esiw'ano (inside your mouth), Feg, King size and Rothmans. Means of administration include smoking, eating, sniffing and brewing into tea.

Cannabis: Wee, Taaba, Abele, Jah, Indian hemp, Marijuana, Taaba, Ahabammono (new leave) Ganja, Panyini, Gari, Hardina, Obonsamtawa, Ntampe, Popoje, Sundu, Tampico, Rolls, Stuff, and Timber. Means of administration include smoking, eating or brewing into tea.

Cocaine: Cracks, Aweabonsonsa, Buu, white powder, energy generator, crazy, maggie powder, soroabofo, snow, coke, Deck (eat it and you'll. be fine), fire on the mountain, hemp and white lady. Means of administration include smoking and sniffing.

Tranquilizers: Blue blue, D5, Valium and Wobeda (you will sleep) Means of administration include swallowing with water or brewing into tea

Heroin: Brown sugar, Vigo, Zimblim, Abibe, Para, Ape and Figure. Means of administration include smoking, sniffing and dissolving in water for injection.

Volatile Inhalants: gases, condensed milk, glue, kerosene, nyamensuo (God's water).

Means of administration include sniffing. For drugs such as amphetamines, opiates and hallucinogens, routes of administration described as smoking, dissolving in water for injection, sniffing, brewing into tea, absorbing into sugar cubes, swallowing and eating. Amphetamines specifically were mentioned as being smoked with tobacco.

Psychoactive drugs are usually grouped into three:

1. Depressants
2. Stimulants
3. Hallucinogens

Depressants include alcohol, barbiturates and heroin. Alcohol is perhaps the most used and abused drug in Nigeria[25]. Alcohol is used to offer prayers in many cultural ceremonies (libation), used for naming new born babies and freely served in wedding occasions in Nigeria. Alcohol is a terrible downer, a sedative depressant of the Central Nervous System. It has been noted to increase violent behavior and a major cause of fatal accident. Heroin is a white powdered substance derived from opium and usually taken by injection. It is a powerful depressant that provides euphoria; the abusers claimed that it is so pleasurable that it can eradicate any thought of food or sex. Barbiturate and sedatives are sleeping pills. Like narcotics, barbiturates exert calming effects on the Central Nervous System.

Stimulants are drugs that excite and sustain activity while diminishing symptoms of fatigue, cigarette, caffeine, amphetamines and cocaine belong to this group. Cocaine is the best known stimulant; it is swallowed, sniffed or injected. Hallucinogens produce hallucinations. These are drugs that induce changes in perceptions, thoughts and feelings; they are usually called "consciousness expanders". The most common hallucinogens in Nigeria are marijuana, known as Indian

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hemp or "Igbo". It produces euphoria and heightens the enjoyment of food, music, sex, etc[22].

g) Level of Substance Abuse

Within the last decade the consumption of substance abuse has drastically increased in Nigeria Hard substances such as alcohol, cannabis, amphetamines among others are now taken frequently and in large quantities by students. The National Drug Law Enforcement Agency can still raise the tempo of its effectiveness by investing heavily on technological device that can enhance its ability to detect drug traffickers or consumers to thwart and frustrate their effort. The annual retrieval of psychoactive substance by prescription is running over five billion gallons of alcohol beverages a year for which some 30_-35million consumers are paying approximately four billion naira.

The level of substance abuse or extent can be classified under three stages:

1) *The Experiment or Recreation Stage:* This is the stage when an individual experiments with the drug at first i.e. the first trial of an individual. The outcome of this stage, determines if the user will continue taking the drugs, or change the drug, continue with the dose he started with he might also consider increasing or reducing the said dose. It is the time when an individual will begin to explore.
2) *Addiction/Habitual Stage:* At this stage, people use drugs to maintain the state of euphoria gotten from the drugs because they have come to like and accept the stage of euphoria they get from the drug. In this stage, the abuser becomes totally dependent on the drug and believes that he can't possibly do anything without the drug because it increases their morale and makes them "high". It can also be referred to as dependence stage it makes the abuser lose control of some situation as they won't be in their right sense without the drug.
3) *Tolerance:* This simply refers to how the abusers system tolerates the drugs. If the drug is well tolerated the abuser can then decide to increase the dose, the frequency at which he takes it.

h) Consequences of Substance Abuse

Drug use by students has hampered education and management in Nigerian secondary schools. In Nigeria, recent statistics suggest that one in every three secondary school students consumes alcohol[1]. Another 8.3% smoke cigarettes while almost one in every ten (9.1%) chew Mira. About 3% smoke bhang and use hard drugs like heroin, cocaine, madras and tranquilizers[12].

Drugs have varied physiological effects. Some adverse consequences include insomnia, prolonged loss of appetite, increased body temperature, greater risk of hepatitis and HIV/AIDS infection death, various forms of cancers, ulcers and brain damage[23]. A study identified accelerated heartbeat, speeding in the peripheral circulation of the blood, alteration of blood pressure, breathing rate and other body functions as potential effects. Cannabis affects the hormonal and reproductive system and the regular use of cannabis can reduce male testosterone and sperm cells[23]. Drug abuse contributes to the formation of uric acid which accelerates conditions like arthritis, gout, osteoporosis, and heart attacks, particularly those with pre-existing coronary hypertensive problems[27]

Drug abuse also affects the brain, resulting in a major decline in its functions. Drugs can affect a student's concentration and thus interest in school and extracurricular activities. This leads to increased absenteeism and drop outs. Most psychoactive drugs affect the decision making process of students, their creative thinking and the development of necessary life and social skills. Drugs also interfere with an individual's awareness of their unique potential and thus their interest in their career development[23].

Drug habits also affect an individual's self-concept. Self-concept refers to the way an individual perceives himself or herself in a variety of areas for example academically, physically, and socially. Low self-esteem can lead to a detrimental redefinition of self-concept and this in turn can lead the student to indulge in escapist behavior such as drug and substance abuse[21]. A study found that when the students are feeling bad about themselves or are feeling unworthy, unloved or rejected, they turn to drugs. Students are affected more by these emotions and their inability to cope given their adolescent stage of development. During this stage, identity formation is important and self-concept plays a major role[21]. Addiction can develop when students' insecurities combine with the influence of peers and the media. Drugs then become the social and emotional focus at the expense of other interests and activities. This gradually leads to social, emotional and physical problems and new feelings of guilt, despair and helplessness.

Therefore, the consequences will be considered in three spheres of life, which includes: Financial, social, and health aspect.

1) *Finiancial Aspect:* The person that is so much addicted to drug tends to spend more money on purchasing drugs like marijuana, tobacco, alcohol, cigarettes, heroine, cocaine e.t.c. This can make the abuser to become bankrupt or start searching for money by all means. For students, they can be forced to spend money that should be used for academic purpose to purchase drugs which might force them to take up odd jobs, make them financially handicapped which can force them to steal. The money used for rehabilitation of victims of substance abuse is also exorbitant.
2) *Health Aspect:* Drugs have varied physiological effects. Some adverse consequences include

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insomnia, prolonged loss of appetite, increased body temperature, greater risk of hepatitis and HIV/AIDS infection, death, various forms of cancers, ulcers and brain damage. A study identified accelerated heartbeat, speeding in the peripheral circulation of the blood, alteration of blood pressure, breathing rate and other body functions as potential effects. Cannabis affects the hormonal and reproductive system and the regular use of cannabis can reduce male testosterone and sperm cells. Drug abuse contributes to the formation of uric acid which accelerates conditions like arthritis, gout, osteoporosis, and heart attacks, particularly those with pre-existing coronary hypertensive problems. It makes them unstable, infiltrates lots of disease into their body such as Hiv/Aids, lung problems, cancers heart problem, cardiac, respiratory, excretory system problem, cirrhosis of the liver, abnormal increase in urine output, and it can make them mentally retarded and eventually make them run mad[21]. Statistical analysis carried out by WHO, about smoking however shows that:

a. Each stick of cigarette a man smoke decreases his life span by eleven minutes
b. Thick smoke in industrial centers can trigger heart attack in two hours.

3) *Social Aspect:* Drug habits also affect an individual's self-concept. Self-concept refers to the way an individual perceives himself or herself in a variety of areas for example academically, physically, and socially[23]. Low self-esteem can lead to a detrimental redefinition of self-concept and this in turn can lead the student to indulge in escapist behavior such as drug and substance abuse. A study[19] found that when the students are feeling bad about themselves or are feeling unworthy, unloved or rejected, they turn to drugs. Students are affected more by these emotions and their inability to cope given their adolescent stage of development. During this stage, identity formation is important and self-concept plays a major role. Addiction can develop when students' insecurities combine with the influence of peers and the media. Drugs then become the social and emotional focus at the expense of other interests and activities. This gradually leads to social, emotional and physical problems and new feelings of guilt, despair and helplessness. Drug abuse also affects the brain, resulting in a major decline in its functions. Drugs like tetrahydrocarbinol (THC), cannabis, alcohol, etc. can affect a student's concentration and thus interest in school and extracurricular activities. This leads to increased absenteeism and drop outs. Most psychoactive drugs affect the decision making process of students, their creative thinking and the development of necessary life and social skills. Drugs also interfere with an individual's awareness of their unique potential and thus their interest in their career development[19].

Other effects of substance abuse include:

a. *Psychological effect:* Although initial drug use may be voluntary, drugs have been shown to alter brain chemistry, which interferes with an individual's ability to make decision and can lead to compulsive craving, seeking, and use which later leads to substance dependency.
b. Behavioral Effect such as paranoia, aggressiveness, hallucinations, addiction, impaired judgment, impulsiveness, loss of self-control, e.t.c.
c. *Peer or Age group effect:* Substance-abusing youth often are alienated from and stigmatized by their peers. Adolescents using alcohol and other drugs also often disengage from school and community activities, depriving their peers and communities of the positive contributions they might otherwise have made.
d. *Effect on relations and families:* In addition to personal adversities, the abuse of alcohol and other drugs by youth may result in family crises and jeopardize many aspects of family life, sometimes resulting in family dysfunction. Both siblings and parents are profoundly affected by alcohol and drug involved youth[20].
e. *Delinquency:* There is an undeniable link between substance abuse and delinquency. Arrest, adjudication, and intervention by the juvenile justice system are eventual consequences for many youths engaged in alcohol and other drug abuse.

Chapter Three

III. Methodology

a) Description of the Study Area

College of Health Science and Technology, Ijero Ekiti is a tertiary institution located in the ancient town of Ijero Ekiti. Ijero Ekiti is a town located in Ekiti State of Nigeria in West Africa. Ijero Ekiti is the headquarters of Ijero Local Government since 1976. The total population of Ijero Ekiti as at 2006 National Population Census was 221,406.

This population can be projected with an annual growth rate of 3.2% to about 221,413 at the end of 2013. The people of Ijero Ekiti are mainly of the Ekiti sub-ethnic group of the Yorubas'. Ijero local government has a state owned School of Health Technology now, College of Health Science and Technology, Ekiti State Cooperative College, Government Technical College Ijero Ekiti and several secondary, primary and nursery schools (both private and government owned).

Various commercial enterprises such as Telecommunication Center, Mobile Network Station,

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Power Holding Company of Nigeria (PHCN), Police Command, Specialist Hospital, Factories, Sawmill, Bakeries, Filling Station, Banks, e.t.c. operate in Ijero Ekiti.

The Ijero local government has a largely agrarian population producing cash crops such as cocoa, kola nuts, coffee, kola, cashew, and timber. The town also produces food crops such as yam, cocoyam, cassava, pepper, tomatoes and bananas, all produced in large quantities with good qualities. The town is also the seat of mineral resources such as tourmaline, colombalt, vesper, and crystal stone.

The College of Health Science and Technology Ijero Ekiti is a state owned tertiary institution which was established as School of Health Technology in 1997 following the creation of Ekiti State in October 1996. The state government believed that there was need to increase the strength of middle-level health personnel in order to supplement the existing manpower in Ekiti state.

Academic programs commenced formally in January 1999 with two courses. They were Community Health Extension Workers (C.H.E.W.) in training and Junior Community Health Extension Workers (J.C.H.E.W.) in training. On 2nd January 2000, the Institution introduced four additional courses. They were Medical Laboratory Assistants (M.L.A.) in training, Pharmacy Technician (P.H.T.) in training, Medical Records Technician (M.R.T.) in training, and Environmental Health Assistant (E.H.A.) in training programmes.

Moreover the long awaited Bill for the establishment of the college was assented to on the 21st of January, 2011. It was a profound experience in the annals of history of the institution that its status by this development, metamorphosed from school to College[31].

b) Advocacy/Community Penetration

Introduction letter was obtained from Pharmacy Technician Department, College of Health Science and Technology, Ijero Ekiti. The letter was taken to the Authorities of College of Health Science and Technology, Ijero Ekiti seeking their permission to carry out the research among the students' in the college premises.

c) Study Population

The study population included all students of College of Health Science and Technology, Ijero Ekiti, whom by the virtue of their provisional admission letter, are students of the College.

d) Inclusion Criteria

All the students of the College who agree to participate in the study were eligible for inclusion in the study.

e) Exclusion Criteria

All students of the College who are not willing to participate in the study were excluded. Students not physically present, or visitors during the data collection process were also excluded.

f) Study Consent

Verbal consent was obtained from the respondents after detailed explanation of the objectives, scope, and benefits of the study had been made known to them.

g) Study Design

A descriptive cross-sectional study design was used for the study.

h) Sample Size Determination

The fisher formula for sample size determination was used to calculate the sample size from the population of student in the college thus:

$$n = \frac{z^2pq}{d^2} \quad \text{and} \quad nf = \frac{n}{1^{+n}/N}$$

Where:

n = desired sample size when total population is $\leq$ 10,000.
z = (standard normal deviation) = 1.96 i.e. 1.96 at 95% confidence level.
p = the knowledge of substance abuse is put at 0.83 (83%)[30].
q = 1.0 – p = 1.0 – 0.83= 0.17
d = degree of accuracy (from the confidence level) set at 0.05 i.e. 5%.
nf = desired sample size when population is < 10,000.
N = estimate of the population size.

i. *Calculations*

$$n = \frac{z^2pq}{d^2}$$

$$= \frac{1.96^2(0.17 \times 0.83)}{(0.05)^2}$$

$$= \frac{3.84 \times 0.141}{2.5 \times 10^{-3}}$$

$$= \frac{5.420 \times 10^{-1}}{2.5 \times 10^{-3}}$$

$$= \frac{5.420 \times 10^{2}}{2.5}$$

$$= \frac{542}{2.5}$$

$$= 216.8$$

$$\approx 217.$$

Since estimated target population is < 10,000

$$nf \textit{ is used} = \frac{n}{1^{+n}/N}$$

$$= \frac{217}{1 + {}^{217}/2{,}904}$$

$$= \frac{217}{1.075}$$

$$= 201.86 \qquad = 202$$

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The minimum sampling required for the study was estimated at 202. However a total of 230 questionnaires were distributed. A total of 220 respondents successfully filled and returned their questionnaires.

i) Sampling Technique

Multistage sampling method was used in the selection of the participants for the study using self-administered questionnaire.

First Stage: The first step was the selection of two-third of the twenty departments in the College of Health Science and Technology, Ijero Ekiti which is 13 departments by using simple random sampling by balloting. The selected 13 departments are;

S/No	Departments	No of Levels	Total
1	Health Education	2	111
2	Bio-Medical Engineering	2	38
3	Health Information Management	3	506
4	Orthopaedic Technician	1	30
5	Community Health Extension Workers	3	156
6	X-ray Technician	3	66
7	Public Health Nursing	2	13
8	Medical Laboratory Technician	3	303
9	Health Technician	3	303
10	Ophthalmic Technician	3	93
11	Pharmacy Technician	3	56
12	Food Hygiene	3	83
13	Dental Health Technician	3	176
14	**GRAND TOTAL**	**34**	**1934**

The second step is the proportional allocation of the sample size across the 13 selected departments within the college thus,

$$\frac{\text{Number of students in each level}}{\text{Total number of students in the 13 selected department}} \times \frac{\text{Sample size}}{1}$$

At Health Education: The two existing levels or arms in Health education department were randomly picked;

100 LEVEL: $\frac{35}{1934} \times 230 = 4$

200 LEVEL: $\frac{76}{1934} \times 230 = 9$

At Bio-Medical Engineering: The two existing levels or arms in Bio-Medical Engineering department were randomly picked.

100 LEVEL: $\frac{15}{1934} \times 230 = 2$

200 LEVEL: $\frac{23}{1934} \times 230 = 3$

At Health Information Management: The three existing levels or arms in Health Information Management department were randomly picked.

100 LEVEL: $\frac{180}{1934} \times 230 = 21$

200 LEVEL: $\frac{150}{1934} \times 230 = 18$

300 LEVEL: $\frac{176}{1934} \times 230 = 21$

At Orthopedic Technician: The only existing level or arm in orthopedic department was picked.

100 LEVEL: $\frac{30}{1934} \times 230 = 4$

At Community Health Extension Worker: The three existing levels or arms in Community Health Extension Worker department were randomly picked.

100 LEVEL: $\frac{50}{1934} \times 230 = 6$

200 LEVEL: $\frac{67}{1934} \times 230 = 8$

300 LEVEL: $\frac{39}{1934} \times 230 = 5$

At X-Ray Technician: The three existing levels or arms in X-ray technician department were randomly picked.

100 LEVEL: $\frac{23}{1934} \times 230 = 3$

200 LEVEL: $\frac{28}{1934} \times 230 = 3$

300 LEVEL: $\frac{15}{1934} \times 230 = 2$

At Public Health Nursing: The two existing levels or arms in Public Health Nursing department were randomly picked.

100 LEVEL: $\frac{5}{1934} \times 230 = 1$

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200 LEVEL: $\frac{8}{1934} \times 230 = 1$

At Medical Laboratory Technician: The three existing levels or arms in Medical Laboratory Technician department were randomly picked.

100 LEVEL: $\frac{120}{1934} \times 230 = 14$

200 LEVEL: $\frac{113}{1934} \times 230 = 13$

300 LEVEL: $\frac{70}{1934} \times 230 = 8$

At Health Technician: The three existing levels or arms in Health Technician department were randomly picked.

100 LEVEL: $\frac{190}{1934} \times 230 = 23$

200 LEVEL: $\frac{84}{1934} \times 230 = 10$

300 LEVEL: $\frac{29}{1934} \times 230 = 3$

At Ophthalmic Nursing: The three existing levels or arms in Ophthalmic Nursing department were randomly picked.

100 LEVEL: $\frac{21}{1934} \times 230 = 2$

200 LEVEL: $\frac{36}{1934} \times 230 = 4$

300 LEVEL: $\frac{36}{1934} \times 230 = 4$

At Pharmacy Technician: The three existing levels or arms in Pharmacy Technician department were randomly picked.

100 LEVEL: $\frac{25}{1934} \times 230 = 3$

200 LEVEL: $\frac{15}{1934} \times 230 = 2$

300 LEVEL: $\frac{16}{1934} \times 230 = 2$

At Food Hygiene: The three existing levels or arms in Food Hygiene department were randomly picked.

100 LEVEL: $\frac{25}{1934} \times 230 = 3$

200 LEVEL: $\frac{29}{1934} \times 230 = 3$

300 LEVEL: $\frac{29}{1934} \times 230 = 3$

At Dental Health Technician: The three existing levels or arms in Dental Health Technician department were randomly picked.

100 LEVEL: $\frac{43}{1934} \times 230 = 5$

200 LEVEL: $\frac{74}{1934} \times 230 = 9$

300 LEVEL: $\frac{59}{1934} \times 230 = 7$

Second Stage: The first step at this stage was the use of systematic random sampling in each of the department thus;

$$\left(\frac{\text{Total number of students in each level}}{\text{Proportion allocated to each level}}\right) = \text{The Sampling Interval.}$$

At Health Education Department sampling interval is:

100 LEVEL: $\frac{35}{4} = 9$

200 LEVEL: $\frac{76}{9} = 8$

Thus, 9 was used as sampling interval for 100 while 8 was used as sampling interval for 200 Level of Health Education Department.

At Bio-Medical Engineering Department sampling interval is:

100 LEVEL: $\frac{15}{2} = 8$

200 LEVEL: $\frac{23}{3} = 8$

Thus, 8 was used as sampling interval for both 100 and 200 Level Bio-Medical Engineering Department.

At Health Information Department sampling interval is:

100 LEVEL: $\frac{180}{21} = 9$

200 LEVEL: $\frac{150}{18} = 8$

300 LEVEL: $\frac{176}{21} = 8$

Thus, 9 was used as sampling interval for 100 Level while 8 was used as sampling interval for both 200, and 300 Level of Health Information Management Department.

At Orthopaedic Department sampling interval is:

100 LEVEL: $\frac{30}{4} = 8$

Thus, 8 was used as sampling interval of 100 Level of Orthopaedic Department.

At Community Health Extension Worker Department sampling interval is:

100 LEVEL: $\frac{50}{6} = 8$

200 LEVEL: $\frac{67}{8} = 8$

300 LEVEL: $\frac{39}{5} = 8$

Thus, 8 was used as sampling interval for 100, 200, and 300 Level of Community Health Extension Worker Department.

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At X-ray Technician Department sampling interval is:

100 LEVEL: $\frac{23}{3} = 8$

200 LEVEL: $\frac{28}{3} = 9$

300 LEVEL: $\frac{15}{2} = 8$

Thus, 8 was used as sampling interval for both 100 and 300 Level while 9 was used as sampling interval for 300 Level of X-ray Technician Department.

At Public Health Nursing Department sampling interval is:

100 LEVEL: $\frac{5}{1} = 5$

200 LEVEL: $\frac{8}{1} = 8$

Thus, 5 was used as sampling interval 100 Level while, 8 was used as the sampling interval of 200 Level of Public Health Nursing Department.

At Medical Laboratory Technician Department sampling interval is:

100 LEVEL: $\frac{120}{14} = 9$

200 LEVEL: $\frac{113}{13} = 9$

300 LEVEL: $\frac{70}{8} = 9$

Thus, 9 was used as sampling interval for 100, 200, and 300 Level of Medical Laboratory Technician Department.

At Health Technician Department sampling interval is:

100 LEVEL: $\frac{190}{23} = 8$

200 LEVEL: $\frac{84}{10} = 8$

300 LEVEL: $\frac{29}{3} = 10$

Thus, 8 was used as sampling interval for both 100 and 200 Level while 10 was used as sampling interval for 300 Level of Health Technician Department.

At Ophthalmic Nursing Department sampling interval is:

100 LEVEL: $\frac{21}{2} = 11$

200 LEVEL: $\frac{36}{4} = 9$

300 LEVEL: $\frac{36}{4} = 9$

Thus, 9 was used as sampling interval for both 200 and 300 Level while 11 was used as sampling interval for 100 Level of Ophthalmic Nursing Department.

At Pharmacy Technician Department sampling interval is:

100 LEVEL: $\frac{25}{3} = 8$

200 LEVEL: $\frac{15}{2} = 8$

300 LEVEL: $\frac{16}{2} = 8$

Thus, 8 was used as sampling interval for 100, 200 and 300 Level of Pharmacy Technician Department.

At Food Hygiene Department sampling interval is:

100 LEVEL: $\frac{25}{3} = 8$

200 LEVEL: $\frac{29}{3} = 10$

300 LEVEL: $\frac{29}{3} = 10$

Thus, 8 was used as sampling interval for 100 Level while 10 was used as sampling interval for both 200, and 300 Level of Food Hygiene Department.

At Dental Health Technician Department sampling interval is:

100 LEVEL: $\frac{43}{5} = 9$

200 LEVEL: $\frac{74}{9} = 8$

300 LEVEL: $\frac{59}{7} = 8$

Thus, 9 was used as sampling interval for 100 Level while 8 was used as sampling interval for both 200, and 300 Level of Dental Health Technician Department.

j) Data Collection

A semi structured self-administered questionnaire was used to collect quantitative data. Questions asked were specific, brief and polite. The questionnaire has four sections with section A relating to the socio-demographic characteristics of the respondents, section B deals with the knowledge that the respondents have about substance abuse together with the substance commonly abused among students, section C is about the level of substance abuse among students and section D concerns with the consequences of substance abuse among students.

k) Data Processing and Analysis

The questionnaires were retrieved, sorted, cleared, checked properly and code entering using the computer. These were later analysed using the SPSS software package. Frequency distribution table and simple percentages were used to present the data. Cross tabulation of important variables was also done. The indices of measurement included the student's involvement in substance abuse.

Chi square test was used to determine the statistical significance of differences in variables observed and p-value was set at $p \leq 0.050$.

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Chapter Four

IV. Results

Section A; Socio-Demographic Characteristics

Table 4.1: Socio- Demographic Characteristics of Respondents (N=220)

Variable	Frequency	Percentage (%)
Age group (in years)(N=220)		
16 – 20	70	31.8
21 – 25	100	45.5
26 – 30	35	15.9
Above 30	15	6.8
Total	220	100
Gender(N=220)		
Male	119	54.1
Female	101	45.9
Total	220	100
Marital Status(N=220)		
Single	156	70.9
Married	54	24.6
Divorced	10	4.5
Total	220	100
LEVEL(N=220)		
100	91	41.4
200	78	35.4
300	51	23.2
Total	220	100
Family Background(N=220)		
Polygamous	157	71.4
Monogamous	63	28.6
Total	220	100
Who they presently live with(N=220)		
Parents	60	27.3
Friends	86	39.1
Alone	74	33.6
Total	220	100

From table 4.1 above, the total number of respondents was 220. Most respondents 100(45.5%) were between the age of 21 -25 years with the least being those that were 30 years and above, 15(6.8%). Minimum age category was 16-20 while maximum age was 30 years and above. There were 91(41.4%) respondents from 100 level, 78(35.4%) from 200 level and 51(23.2%) from 300 level. There were more male respondents 119(54.1%) than the females101 (45.9%). Out of the total 220 correspondents 156(70.9%) were single, 54(24.6%) were married and 10(4.5%) accounts for divorced couple. 157(71.4%) accounts for respondents of polygamous family background while 63(28.6%) accounts for those of monogamous family background. 60(27.3%) live with their parents while 86(39.1%) live with their friends and 74(33.6%) live alone.

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Section B: Knowledge of Substance Abuse

Table 4.2: Shows Respondents Source of Knowledge on Substance Abuse

Variable	Frequency	Percentage (%)
Source of information on substance abuse(N=220)		
Hospital	25	10.9
Radio	20	8.7
Television	35	15.3
Poster	20	8.7
Friend	58	25.4
School	40	17.5
Seminar	15	6.5
Others(multiple choice)	15	6.5
Involvement in substance abuse(N=220)		
Yes	150	68.2
No	70	31.8
Total	220	100
Knowledge of health hazard associated with taking drugs without doctor's prescription(N=220)		
Yes	115	52.3
No	105	47.7
Total	220	100
Increased efficiency due to substance abuse(N=150)		
Yes	120	80.0
No	30	20.0
Total	150	100
Substances frequently abused(N=150)		
Cigarette	15	10.0
Opioids	30	20.0
Amphetamines	25	16.7
Alcohol	80	53.3
Total	150	100

Table 4.2 shows that 25(10.9%) people heard of substance abuse from hospital, while 20(8.7%) heard from radio, 35(15.3%) heard from television, 20(8.7%) from poster, 58(25.4%) from friends, 40(17.5%) from school, 15(6.5%) from seminar, while 15(6.5%) heard from more than one source. Also, 15(10%) are familiar with cigarette while 30(20%) are familiar with opioids, 25(16.7%) are familiar with amphetamines while 80(53.3%) are familiar with alcohol. A total of 150(80%) are involved in substance abuse while 70(20%) aren't.

Out of the 150 that are involved in substance abuse, 120(80%) experiences increased efficiency while 30(20%) claims not to experience.

Section C: Level of Substance Abuse

Table 4.3: Shows the Level of Substance Abuse among Students

Variable	Frequency	Percentage (%)
Time it took to adapt(N=150)		
Days	97	64.7
Weeks	30	20.0
Months	23	15.3
Total	150	100
Administration of specific dose(N=150)		
Yes	115	76.7
No	35	23.3
Total	150	100
Route of Administration(N=150)		
Orally	90	60.0
Parenteral	45	30.0
Inhalation	15	10.0
Total	150	100
Frequency of Consumption(N=150)		
Daily	117	78.0
Hourly	23	15.3
Weekly	10	6.7
Total	150	100

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Table 4.3 shows that 97(64.7%) adapted to this drugs in a number of days while 30(20.0%) took weeks to adapt to the drug and about 23(15.3%) took months to adapt to the drug. The most frequent route of administration was orally which accounts for 90(60.0%), then parenteral route which accounts for 45(30.0%) then inhalation 15(10.0%). Frequency of consumption figured out to be 117(78.0%) daily, Hourly 23(15.3%), and weekly 10(6.7%).

Section D: Effects of Substance Abuse

Table 4.4: Shows the Consequences of Substance Abuse

Variable	Frequency	Percentage (%)
Academic Performance Rate(N=220)		
Fair	60	27.3
Average	40	18.2
Good	60	27.3
Very Good	30	13.6
Excellent	30	13.6
Total	220	100
Progression in performance after consuming substance(N=150)		
Yes	30	20.0
No	120	80.0
Total	150	100
Source of money to purchase substance(N=150)		
School fee	23	15.3
Odd jobs	47	36.4
Parents	80	40.9
Multiple choice	7	3.2
Financial instability due to substance abuse(N=150)		
Yes	92	61.3
No	58	38.7
Total	150	100
Those that have been asked to cut down intake(N=150)		
Yes	95	63.3
No	55	36.7
Total	150	100
To what extent		
Minimal	38	40.0
Total Abstinence	57	60.0
Total	95	100

Out of 220 respondents, 60(27.3%) were rated fair in their academic performance, 40(18.2%) were rated average, and 60(27.3%) are rated good in their academic performance while 30(13.6%) are rated very good, a total of 30(13.6%) were rated excellence on their academic performance. Result also shows that 23(15.3%) got money to source for the drug from school fees, 47(36.4%) through friends while 80(40.9%) got money through odd jobs.

The analysis shows that 120(80%) did not experience any progression in their academic performance, and 30(20%) did experience progression in their academics. It was revealed that 92(61.3%) were affected financially while 58(38.7%) were not. Findings also shows that 95(63.3%) have been advised to cut down the intake of any substance they might be consuming and 55(36.7%) have not received such advice.

The table further reveals that 57(60%) have been advised to abstain totally from substances while 38(40%) have been advised to reduce the intake to its minimal level.

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Section E: Cross Tabulation.

Table 4.5: Cross Tabulation between the gender of respondents and their involvements in substance abuse

Gender	Involvement		Chi-square	Degree of freedom	P-value
	Yes	No			
Male	113(97%)	6(3%)	85.868	1	0.000
Female	37(36.6%)	64(63.4%)			

Table 4.5 shows that more males were involved were involved in substance abuse than their female counterparts. The difference was however statistically significant as its p- value of 0.000 is less than the 0.050 alpha level of significance.

Table 4.6: Cross Tabulation between Age of respondents and their involvement in substance abuse

Age group	Involvement		Chi-square	Degree of freedom	P-value
	Yes	No			
16 – 20	43(61.4%)	27(38.6%)	6.883	3	0.100
21 – 25	75(75%)	25(25%)			
26 – 30	25(71.4%)	10(28.6%)			
30 and above	7(46.7%)	8(53.3)			

Table 4.6 shows that respondent between the age of 21 -25 are more involved in substance abuse than respondents from other age group, this finding is not statistically significant because its p-value of 0.100 is greater than the 0.050 alpha level of significance

Table 4.7: Cross Tabulation between Marital Status of respondents with their involvement in substance abuse

Marital Status	Involvement		Chi-square	Degree of Freedom	P-value
	Yes	No			
Single	118(75.6%)	38(24.4%)	15.876	2	0.000
Married	25(46.3%)	29(53.7%)			
Divorced	7(70%)	3(30%)			

Table 4.7 shows that respondent with marital status of single are more involved in substance abuse than respondents from other categories, this finding is however statistically significant because its p-value of 0.000 is less than the 0.050 alpha level of significance

Table 4.8: Cross Tabulation between the level of respondents to their involvements in substance abuse

Level	Involvement		Chi-square	Degree of Freedom	P-value
	Yes	No			
100	70(76.9%)	21(23.1%)	4.709	2	0.025
200	49(62.8%)	29(37.2%)			
300	31(60.8%)	20(39.2%)			

Table 4.8 shows that respondents from 100 level are more involved in substance abuse than respondents from other departmental level, the table revealed that the observation is statistically significant because its p-value of 0.025 is less than the 0.050 alpha level of significance

Table 4.9: Cross Tabulation between family background of respondent to their involvement in substance abuse

Family Background	Involvement		Chi-square	Degree of Freedom	P-value
	Yes	No			
Polygamous	108(68.8%)	49(31.2%)	0.102	1	0.975
Monogamous	42(66.7%)	21(33.3%)			

Table 4.9 shows that respondents from polygamous family are more involved in substance abuse than respondents monogamous family, this finding is not statistically significant because its p-value of 0.975 is greater than the 0.050 alpha level of significance.

Table 4.10: Cross Tabulation between departmental level to their knowledge of substance abuse

Departmental Level	Knowledge of substance abuse		Chi-square	Degree of Freedom	P-value
	Yes	No			
100	40(78.4%)	11(21.6%)	3.256	2	0.200
200	50(64.1%)	28(35.9%)			
300	60(65.9%)	31(34.1%)			

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Table 4.10 shows that respondent in 300 level have the knowledge of substance abuse more than respondents from other departmental levels, this finding is not statistically significant because its p-value of 0.200 is greater than the 0.050 alpha level of significance

Table 4.11: Cross Tabulation between who they presently live with and their level of substance abuse (frequency of consumption)

Who they presently live with	Frequency of Consumption			Chi-square	Degree of Freedom	P-value
	Hourly	Daily	Weekly			
Parents	6(16.7%)	12(33.3%)	18(50%)	22.748	4	0.000
Friends	20(31.3%)	30(46.9%)	14(21.9%)			
Alone	30(60%)	10(20%)	10(20%)			

Table 4.11 shows that respondents that live alone has a higher frequency of consumption than respondents from other categories, this finding is however statistically significant because its p-value of 0.000 is less than the 0.050 alpha level of significance

Chapter Five

V. Discussion

For the assessment of substance abuse among the students of College of Health Sciences and Technology Ijero Ekiti, 230 questionnaires were distributed among the students of the 13 selected departments; however, a total of 220(95.65%) questionnaires were retrieved.

The total number of respondents was 220. Most respondents 100(45.5%) were between the age of 21 - 25 years with the least being those that were 30 years and above 15(6.8%). Minimum age category was 16-17 years while maximum age was above 30. There were 91(41.4%) respondents from 100 level, 78(35.4%) from 200 level and 51(23.2%) from 300 level. There were more male respondents 119(54.1%) than the females101 (45.9%). Out of the total 220 correspondents 156(70.9%) were single, 54(24.6%) were married and 10(4.5%) accounts for divorced couple. 157(71.4%) accounts for respondents of polygamous family background while 63(28.6%) accounts for those of monogamous family background. 60(27.3%) live with their parents while 86(39.1%) live with their friends and 74(33.6%) live alone.

Further analysis of data shows that 25(10.9%) student heard of substance abuse from hospital, while 20(8.7%) heard from radio, 35(15.3%) heard from television, 20(8.7%) from poster, 58(25.4%) from friends, 40(17.5%) from school, 15(6.5%) from seminar, while 15(6.5%) heard from more than one source. Also, 15(10%) are familiar with cigarette while 30(20%) are familiar with opioids, 25(16.7%) are familiar with amphetamines while 80(53.3%) are familiar with alcohol. A total of 150(80%) are involved in substance abuse while 70(20%) aren't. Out of the 150 that are involved in substance abuse, 120(80%) experiences increased efficiency while 30(20%) claims not to experience.

Findings revealed that 97(64.7%) adapted to this drugs in a number of days while 30(20.0%) took weeks to adapt to the drug and about 23(15.3%) took months to adapt to the drug. The most frequent route of administration was orally which accounts for 90(60.0%), then parenteral route which accounts for 45(30.0%) then inhalation 15(10.0%). Frequency of consumption figured out to be 117(78.0%) daily, Hourly 23(15.3%), and weekly 10(6.7%).

Out of 220 respondents, 60(27.3%) were rated fair in their academic performance, 40(18.2%) were rated average, and 60(27.3%) are rated good in their academic performance while 30(13.6%) are rated very good, a total of 30(13.6%) were rated excellence on their academic performance. Result also shows that 23(15.3%) got money to source for the drug from school fees, 47(36.4%) through friends while 80(40.9%) got money through odd jobs. Out of the 150 respondents that are involved in substance abuse, 120(80%) did not experience any progression in their academic performance, and 30(20%) experience progression in their academics. It was revealed that 92(61.3%) were affected financially while 58(38.7%) were not. Findings also shows that 95(63.3%) have been advised to cut down the intake of any substance they might be consuming and 55(36.7%) have not received such advice, 57(60%) have been advised to abstain totally from substances while 38(40%) have been advised to reduce the intake to its minimal level.

Further analysis shows that out of the 150 respondents that are involved in substance abuse more males were involved in substance abuse than their female counterparts, reason being that they believe that, the males abuse substance for effective performance in various spheres of life (sex which can induce the use of substance such as aphrodisiac , effectiveness in work such as hard labour which can also induce the abuse of tramadol, and to increase academic performance by taking substance such as nescafe which contains high proportion of caffeine for night classes. The difference was however statistically significant as its p- value of 0.000 is less than the 0.050 alpha level of significance.

Respondent between the age of 21 -25 are more involved in substance abuse than respondents

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from other age group, this finding is not statistically significant because its p-value of 0.100 is greater than the 0.050 alpha level of significance.

Respondent with marital status of single are more involved in substance abuse than respondents from other categories, this is because those that are single are with little or no responsibility, this finding is however statistically significant because its p-value of 0.000 is less than the 0.050 alpha level of significance.

Respondents from 100 level are more involved in substance abuse than respondents from other level, this is because the freshers are new to the school environment and they want to try out every experience and it is also due to misconception, the table revealed that the observation is statistically significant because its p-value of 0.025 is less than the 0.050 alpha level of significance.

Respondents from polygamous family are more involved in substance abuse than respondents monogamous family, this means that the family background of the respondent has a great impact on the involvement of respondents in substance abuse, this finding is not statistically significant because its p-value of 0.975 is greater than the 0.050 alpha level of significance.

Respondent in 300 level have the knowledge of substance abuse more than respondents from other levels, this is because their level of perception of substance abuse is high, this finding is not statistically significant because its p-value of 0.200 is greater than the 0.050 alpha level of significance.

Respondents that live alone has a higher frequency of consumption than respondents from other categories, because they free to do whatever they want without any interruption, this finding is however statistically significant because its p-value of 0.000 is less than the 0.050 alpha level of significance.

Chapter Six

VI. Conclusion

Drug abuse is a problem that is of a great concern to the society and the government at large. The problem is prevalent among youth who in most cases are ignorant about the dangers inherent in drug abuse. Many of them are involved in drug abuse due to lack of parental supervision, frustration. Peer pressure, poverty, pleasure etc. which can lead to juvenile delinquencies However, with effective counselling program this problem can be curbed and tracked. Based on the findings previously reported in this study, the following conclusions were drawn.

* The use of alcohol is the most common dangerous substance (drug) abuse.
* Peer group are the major people who influence the use of substance (drug).
* Substance abuse is a problem among the students of college of health sciences and technology ijero- Ekiti
* People take substance (drug) for a number of reasons: to treat body ailment, to prolong wakefulness, for relaxation, to avoid emotional trauma, to forget about their problem, to satisfy curiosity, to cope with peer pressure among others.

a) Recommendations

We have by now analysed the major findings of the survey, and interpreted the quantitative data with the help of qualitative data collected from focus group sessions (students of college of health sciences and technology). In so doing, we have already fulfilled the objectives of the study which are

1) To determine the knowledge of substance abuse among students of college of health sciences and technology
2) To determine the substances common abused among students of college of health sciences and technology
3) To determine level of substance abuse among students of the college
4) To determine consequences of substance abuse

Our final task is to make some broad recommendations, on the basis of findings of the study, for possible improvement of existing programs in rehabilitation and related services for students involved in substance abuse.

In view of the highlights of this study, the following recommendations are suggested to curb, reduce, or control drug abuse among youth.

- Designing curricula on drug education; ministry of education at all level (Local, State, and federal) should as a matter of urgency add d curricula of drug education to all level of education
- Educative posters and advertisements on every media platform to constantly remind people on the negative effects of drug abuse
- Establishment of counselling centres on drug abuse
- Establishment of rehabilitation centres to cater for those that have been affected
- Drug law enforcement agencies should wake up to their responsibility so as to control drug trafficking
- These agencies should be strengthened to punish drug users
- Drug abuse should be rated as an offence punishable by law.
- Voluntary organization and service clubs must be encourage in the society to render useful service where necessary, so as to divert people mind from evil practice and bad peer group

It is further recommended that law enforcement agencies (NAFDAC, NDLEA, e.t.c.) need to work in tandem so as to curb the problem of substance abuse in our society and

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Further Recommendations Includes:

► Raising Self-Efficacy

Self-efficacy is the individual's perceived ability to resist the temptation to re-use a drug even in a high-risk situation, such as sighting of the drug.

The prominence of self-efficacy in affecting the length of abstinence of chronic drug abusers sends the strong signal that strengthening the self-efficacy of students would be one of the most effective means to improve rehabilitation programs and services. It is advised that most programs attach importance to developing self-efficacy in their clients (students). We suggest that programs of different modalities can review the elements in their programs that aim to improve self-efficacy, and review their effectiveness. Whatever the new strategies that may be introduced into programs, they must teach the students to assess their actual level of self-efficacy, so that they would not mistakenly put themselves at risk by over-estimating their ability to "stay firm" in a situation beyond their self-efficacy can handle.

► Building Social Network in Treated Addicts

Association with drug-using friends and support from non-drug-using friends significantly influence the students' performance in the intervals of the study. Both involve the re-establishment of social relations after leaving the treatment setting. Social relations can generate resources that can be used to facilitate social goals. Re-entering a network of drug-using friends would generate *negative social capital*, thereby undermining self-efficacy and reducing the ability to be drug-free. On the contrary, re-establishing a network of non-drug-using friends who can lend their support would generate *positive social capital*, protecting the subject from re-associating with drug-using friends, increasing self-efficacy, and finally contributing to reaching the goal of maintaining drug-free status. The implication of this finding is obvious. How a treated addict re-organizes or re-establishes his/her social circle is a crucial juncture in his/her pathway to recovery/relapse.

Most of the present programs would remind students to stay away from former Drug-using friends. But some students would go back to live in their original drug Neighbourhood if no new arrangements of location are made for them after leaving the Program. Those programs that are able to help treated clients to acquire collective rental accommodations far from their original neighbourhood do offer a better protective measure for the student. In order to better protect treated addicts against re-associating with drug-using friends, the collaboration of other agencies and government departments would be necessary. For example, the Housing Department may help to make it easier for this group of people to be re-located to other districts under the Compassionate Re-housing Scheme.

To compete with drug-using friends in winning the treated addicts, many programs have organized social activities for treated clients to socialize with ex-addicts and to help each other and are extremely useful in helping treated addicts to stay away from the danger of re-association with drug-using peers, and in facilitating the re-learning and re-practicing of a normal life among treated students, through either informal interaction or more structured recovery training.

All of these aftercare efforts are paramount to the building of positive social capital in treated addicts. More should be done to expand existing strategies, develop new and innovative ones, so that more social capital can be generated for use by treated clients.

► Facilitating Satisfaction with Life

While the life of treated addicts is full of hardship, the dissatisfaction with life Induced by relative deprivation can be even more destructive than material shortage.

Treated addicts must be taught to reset their aspiration levels, so that there is a balance between what they are able to achieve and the achievements they aspire to.

Inculcating a realistic aspiration level in them can facilitate more satisfaction of life, which would in turn result in longer abstinence. How to effectively help treated addicts to identify realistic goals and be satisfied with them is a big challenge to counselors of existing programs. Addicts in different stages of addiction or stages of life would have different abilities, needs, and aspirations. An important step is to assess the different needs and abilities of addicts in different stages of life, and then help them to meet their needs, and foster their abilities to achieve their goals, in the context of realistic aspirations. Therefore, there is a need to create awareness of the fact that certain goals can still be achieved after rehabilitation process.

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Appendix I

College of Health Science and Technology, Ijero Ekiti Department of Pharmacy Technician. Questionnaire

An Assessment of Substance Abuse among Students of College of Health Science and Technology Ijero Ekiti.

The research is a required academic exercise; therefore all gathered information shall only be used for academic reasons. Your anonymity is highly guaranteed, provision of true information can advance the knowledge. Thanks for your anticipated co-operation.

Instruction: Tick (✓) as appropriate please.

Section A

1. Sex: Male ( ), Female ( )
2. Age: 16 – 20 ( ), 21 – 25 ( ), 26 – 30 ( ), 30 and above ( )
3. Marital Status: Single ( ), Married ( ), Divorce ( )
4. Department: _____

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5. Level: 100 ( ), 200 ( ), 300 ( ).
6. What kind of family are you from? Polygamous ( ), Monogamous ( ), Others specify_____
7. Who do you presently live with? Father ( ), Mother ( ), Friend ( )

Section B: To Assess the Knowledge of Substance Abuse

8. Have you heard anything about substance abuse before? Yes ( ), No ( )
9. If yes to question 8 above, from which source? Hospital ( ), Radio ( ), Television ( ), Poster ( ), Friends ( ), School ( ), Seminar/Workshop ( ), Others specify_____
10. If yes to question 8 above, what is your view about substance abuse__
11. Have you ever been involved in drug abuse before? Yes( ), No( )
12. If yes to 11 how do you source for the drug? _____
13. Did you know that taking drugs without doctor's prescription could be dangerous to your health? Yes ( ), No( )
14. Which of these substances are you familiar with: cigarette ( ) opioids( ) Amphetamines( ) Alcohol( )

Section C: To Determine the Level of Substance Abuse among Students.

15. Do you feel better or work efficiently if you don't take the substance? Yes ( ), No ( )
16. How do you feel if you take any of it? High morale ( ), increased energy ( ), increased efficiency ( ), others specify ( ).
17. Can you perform any task if you don't take it? Yes( ), no( )
18. Did you react to the drug when you took your first shot? Yes ( ) no ( )
19. How long did it take you to adapt to the substance? Days ( ), Weeks ( ), month ( )
20. Do you have a specific dose that you take? Yes ( ), No ( )
21. How do you administer or take the drug_____
22. Do you feel sick if you don't take the substance? Yes ( ), No ( )
23. Do you take it in large quantity? Yes ( ), No ( )
24. How often do you consume it? Hourly ( ) Daily ( ) weekly ( )

Section D: Consequences of Substance Abuse among Students of Cohest

25. How would you rate your performance at school Fair ( ), Average ( ), Good ( ), Very good ( ) Excellent ( )
26. Has there been any progression in your performance since you started taking the substance Yes ( ), No ( )
27. Where do you get money to purchase it? School fee ( ), Friends ( ), Odd jobs ( ), others specify ( ).
28. Do you believe that taking alcohol can affect you financially? Yes ( ), No ( )
29. Have you been diagnosed of any ailment since you started taking the substance? Yes ( ), No ( )
30. If yes to question 29 above specify_____
31. Has your physician ever advised you to cut down the intake of such substance? Yes ( ), No( )
32. If yes to what extent? Minimal ( ), Total abstinence ( )

Appendix II

Total Population of Students in College of Health Sciences and Technology, Ijero Ekiti

Department	100 Level	200 Level	300 Level	400 Level	Total
Pharmacy Technician	25	15	16	----	56
Medical Laboratory Technician	120	113	70	----	303
X-Ray Technician	23	28	15	----	66
Health Information Management	180	150	176	----	506
Opthalmic Technician	21	36	36	----	93
Biomedical Engineering	15	23	----	----	38
Health Technician	190	84	29	----	303
Dental Health Technician	43	74	59	----	176
Public Health Nursing	5	8	----	----	13
Orthopedic	30	----	----	----	30
Community Health Extension Workers	50	67	39	----	156
Junior Community Health Extension Workers	50	65	----	----	115
Human Nutrition Department	17	29	45	----	91
Occupational Health And Safety	2	5	7	----	14
Health Education	35	76	----	----	111
Food Hygiene	25	29	29	----	83
Environmental Health Technician	75	71	64	----	210
Environmental Health Technology	94	80	87	84	345
Environmental Health Assistant	35	40	----	----	75
Remedial					120
	Grand Total				2,904

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Appendix III

P-value Table

	I_P										
DF	**0.995**	**0.975**	**0.20**	**0.10**	**0.05**	**0.025**	**0.02**	**0.01**	**0.005**	**0.002**	**0.001**
1	0.0000393	0.000982	1.642	2.706	3.841	5.024	5.412	6.635	7.879	9.550	10.828
2	0.0100	0.0506	3.219	4.605	5.991	7.378	7.824	9.210	10.597	12.429	13.816
3	0.0717	0.216	4.642	6.251	7.815	9.348	9.837	11.345	12.838	14.796	16.266
4	0.207	0.484	5.989	7.779	9.488	11.143	11.668	13.277	14.860	16.924	18.467
5	0.412	0.831	7.289	9.236	11.070	12.833	13.388	15.086	16.750	18.907	20.515
6	0.676	1.237	8.558	10.645	12.592	14.449	15.033	16.812	18.548	20.791	22.458
7	0.989	1.690	9.803	12.017	14.067	16.013	16.622	18.475	20.278	22.601	24.322
8	1.344	2.180	11.030	13.362	15.507	17.535	18.168	20.090	21.955	24.352	26.124
9	1.735	2.700	12.242	14.684	16.919	19.023	19.679	21.666	23.589	26.056	27.877
10	2.156	3.247	13.442	15.987	18.307	20.483	21.161	23.209	25.188	27.722	29.588

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Antihypertensive and Antiatherogenic Effects of *Tanopati* a Traditional Recipe used for the Treatment of High Blood Pressure

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Abstract- *Background:* The objective of the present study was to investigate the possible effect of Tanopati on induced hypercholesterolemia in rats and hypertension in rabbits.

Methods: Twenty wistar rats were divided into 4 groups each and then subjected to different treatments. Hypercholesterolemia was induced by induced dietary cholesterol; the rats are then treated with Tanopati and Questran®)

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Keywords: *tanopati, antihypercholesterolemia, cardiovascular index, adrenaline.*

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Antihypertensive and Antiatherogenic Effects of *Tanopati* a Traditional Recipe used for the Treatment of High Blood Pressure

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Results: The treatment with the Tanopati and with Questran® significantly improved ($p < 0.05$) these parameters by decreasing the concentrations of total cholesterol, triglyceride and LDL-cholesterol against an elevation of HDL cholesterol levels. After 8 days of treatments on rabbits induced hypertension with *Tanopati* or with Tenordate®, cardiovascular parameters decreased significantly up to their normalization values.

Conclusions: The results obtained confirm the antihypertensive effect of Tanopati and justify it traditionally use in treatment of high blood pressure.

Keywords: tanopati, antihypercholesterolemia, cardiovascular index, adrenaline.

I. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality worldwide and hypertension remains the most common cardiovascular disease and a major public health issue in both developed and developing countries.[1]

Hypertension, according to the National High Blood Pressure Education Program (NHBPEP), is defined as systolic blood pressure (SBP) equal or greater than 140 mmHg and diastolic blood pressure (DBP) as equal or more than 90 mmHg, taking antihypertensive medication, or being told twice by a physician or other professional that one has hypertension. It is also defined as a condition in which the arterial blood pressure is chronically elevated. Hypertension is considered an independent, useful and powerful prognostic indicator for cardiovascular and renal disease, whereas it is significantly associated with the increased morbidity and mortality from cerebrovascular disease, myocardial infarction, congestive heart failure and renal insufficiency.[1] Various studies indicate that high levels of serum cholesterol are closely linked to atherosclerosis and increased risk of various cardiovascular diseases.

Cardiovascular diseases, including coronary heart disease, stroke (stroke) and hypertension have some major health threats worldwide today. High plasma lipids (hyperlipidemia and other abnormal blood lipid profile) are among the risk factors commonly involved in most cardiovascular problems.

Under these conditions, lipids and other related substances accumulate on the arterial wall, forming a plate which occludes the lumen and obstructs blood flow to vital organs such as the heart, brain, liver, or kidneys. Lipids with significant elevations are involved in these diseases are cholesterol and triglycerides. They are generally transported in the form of lipid-protein complexes called lipoproteins, which are classified according to their density and their loads. Cholesterol and high density lipoprotein (HDL-C) transports lipid blood cells in the liver, while the low-density lipoprotein cholesterol (LDL-C) mobilizes lipids in the cells and blood vessels. The increased levels of triglycerides, total cholesterol and LDL-C and HDL-C reduction promote the development of atherosclerosis and related cerebrovascular disorders.

The treatment management is usually a lifelong treatment and the cost of treatment is not affordable to the majority of the developing countries population that has recourse to a recipe from medicinal plants.

In the last three decades, a lot of concerted efforts have been channeled into researching into local plants with hypotensive and antihypertensive therapeutic

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values, with the therapeutic potentials of some of these medicinal plants either validated or outrightly disproved. However, attempts by the low-income group, particularly the rural dwellers in the developing countries, to control hypertension and its attendant complications in the face of the scarce socioeconomic resources, have led more people opting for herbal remedy.[2]

Identification of antihypertensive foods and herbal remedies is currently interested because they are expected to prevent hypertension with lower side-effects than antihypertensive drugs.[3] But, these drugs have various side effects that could lead to the malfunctioning of the body function e.g. formation of gall stones, gall bladder diseases, itching and diarrhea. Therefore, much attention has been shifted to the use of natural products from plants with very few side effects in the treatment of atherosclerosis.[3] The mechanisms of these products are elicited to counteract the effect of hypertension and associated risk factors such as hypercholesterolemia, hypertriglyceridemia, and oxidative stress on blood vessel walls. They include direct vasodilation of the blood vessel, blocking of calcium channels, inhibition of α-adrenoreceptor response, induction of negative ionotropic response of smooth muscle, inhibition of platelet aggregation, reduction of vascular resistance, and improvement of pulmonary oxygen utilization.[4]

Enhanced activity of nitric oxide and improved handling of intracellular calcium has also been found to play a critical role in the reduction of vascular resistance and blood pressure that are elevated in hypertensive rats and humans.[5]

Many researchers are actively looking for antihypertensive compounds derived from various natural products for the use in functional foods. Several studies have shown that food ingredients rich in flavonoids and other polyphenols can lower blood pressure.[6] Ours earlier studies have demonstrated that the extract of *Tanopati*, a polyherbal formulation used in treatment of high blood pressure is rich in phenolic compounds such as tannins, flavonoids, leucoanthocyans, anthocyans.[7]

The aim of the present study was to investigate the possible effect of *Tanopati* on induced hypercholesterolemia in rats and hypertension in rabbits.

II. Methods

a) Chemicals

Quesran®, was obtained from a pharmaceutical company in Abidjan (Cote d'Ivoire). HDL –Cholesterol, Total Cholesterol and Triglyceride Kits, Potassium Phosphate buffer and Cholesterol, were obtained from Roche Diagnostics (France).

b) Plant material

The plant material is a recipe obtained from the decoction of roots, leaves and bark of ivorian traditional medicine plants. These are: *Ageratum conyzoides, Newbouldia laevis, Phyllanthus muellerianus, Aloe vera* and *Cassia occidentalis*. This recipe was appointed by the health *Tanopati* traditional healer.

c) Animals

Male's wistar rats weighing 150-200 g procured from the animal house of the faculty of pharmaceutical and biological sciences, Félix Houphouet-Boigny University of Abidjan. Rabbits males' of the species *Oryctolagus cuniculus*, aged 10 weeks weighting 1800 to 2200 g were used. These animals were brought from a poultry farm in Abidjan, were acclimated for two weeks at the Animal unit of the faculty of pharmaceutical and biological sciences, Félix Houphouet-Boigny University of Abidjan. All these animals were housed in plastic cages where they had free access to water and food, and kept at a temperature of 22±3° C with a relative humidity of 50.15%. The cycle of light and darkness was 12 h/12 h. All the experimental procedures were approved by the Ethical Committee of Health Sciences, Félix Houphouet- Boigny University of Abidjan. These guidelines were in accordance with the European Council Legislation 87/607/EEC for the protection of experimental animals.

d) Preparation of lyophilized extract Tanopati

This recipe was provided by M. Adou Tano Albert, an Ivorian traditional practitioner. The decoction was then lyophilized and stored in the freezer for the study.

e) Evaluation of antiatherogenic activity of lyophilized extract Tanopati

This study was to induce hypercholesterolemia with dietary cholesterol and to evaluate the antihypercholestérolémic effect of *Tanopati* using Questran® as reference product.

f) Experimental Protocol

The experiment was conducted according to the method of Erukainure et al.[8]

Twenty (20) male albino rats were divided into 4 groups of 5 animals each and then subjected to different treatments.

- Group 1 (normal control) has received from corn oil (0.3 ml / rat) throughout the experiment.
- Group 2 (experimental control) RCU has only cholesterol (40 mg/kg bw) for the duration of the experiment.
- Group 3 *(Tanopati*) has received cholesterol (40 mg/kg bw) then *Tanopati*
- Group 4 (Questran®) has received cholesterol (40 mg / kg BW) followed Questran® (260 mg/kg bw).

The administration of Questran®, *Tanopati*, and cholesterol were given orally 5 times a week for 6 weeks using an intragastric tube to the volume of 5 mL/kg bw. Corn oil was used as a vehicle to *Tanopati*, Questran®

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and cholesterol. The dose of the extract of *Tanopati* was calculated from the dosage given by the health tradipractitioner.

At the end of 6 weeks of treatment, animals were sacrificed under light anesthesia with ether vapor. The blood collected in EDTA tubes was centrifuged at 3000 revs/min for 10 min and the supernatant (plasma) was used for the determination of total cholesterol, HDL cholesterol and triglycerides.

g) Estimation of biochemical parameters of interest

Total cholesterol was assayed by the method of cholesterol oxidase (CHOD)/peroxidase (POD).[9] HDL cholesterol was measured by the method precipitation.[10] The concentration of serum LDL is determined by the difference method of the equation by Friedewald et al.[11] Triglycerides were assayed by the method of the oxidase glycerol 3-phosphate (GPO)/peroxidase (POD).[12]

The atherogenic index was calculated by the following formula:

$$Atherogenic\ index = \frac{\text{Cholesterol total}}{\text{Cholesterol HDL}}$$

h) Effect of Tanopati on blood pressure and heart rate

i. *Chemicals and drugs*

Adrenalin and Ténordate® were obtained from local office, Abidjan, Cote d'Ivoire, *Tanopati* was gifted by an Ivorian traditional practitioner, all reagents, solvents and chemical compounds used for analysis met the quality criteria in accordance with international standards

ii. *Experimental protocol*

The experiment was performed by the method described by Tiekpa et al.[13] Sixteen (16) male rabbits were divided into 4 lots of 4 rabbits (Lot1to 4). Lot 1 or witness lot received throughout the duration of the experiment distilled water; Lot 2-6 or experimental lots were intramuscularly injected with an insulin syringe, adrenaline dosed at 1 mg/ml to cause elevated blood pressure or hypertension, which was later stabilized after 14 days of treatment. Blood pressure of rabbits was taken with an electric manometer which cuff was adapted to the leg of rabbit. The cuff was wrapped around the left hide leg of the animal and its inflation gauge enabled with the on button. The cuff inflates to the maximum to tighten up the leg of the animal and deflates immediately. It appears on the manometer screen, systolic pressure, diastolic pressure and the heart rate of rabbit. These three cardiovascular parameters of rabbits were then compared to the witness group. After induction of hypertension in animals, they were treated with the *Tanopati* and Ténordate® a reference antihypertensive sold in the market. Each lot was treated as follows:

LOT 1: Witness + distilled water
LOT 2: Witness treated with adrenaline (Adr)
LOT 3: Treated with Adrenalin + Ténordate® (Atenolol +Nifedipine) (10 mg/kg bw)
LOT 4: Treated with Adrenalin + *Tanopati* (10 mg/kg bw)

i) Statistical analysis

The results are expressed as mean±SEM. The results were analyzed using one-way ANOVA followed by Turkey's multiple comparison tests. Data was computed for statistical analysis by using graph pad prism 5 Software. P values <0.05 were considered as significant.

III. Results

a) Effect of the extract of Tanopati on induced hypercholesterolemia in rats

The results show that plasma concentrations of total cholesterol, triglyceride and LDL cholesterol were significantly higher ($p < 0.05$) in the group addicted to dietary cholesterol, while HDL cholesterol rate is lower than the normal group control. The treatment with the Questran® and *Tanopati* significantly improved ($p < 0.05$) these parameters by decreasing the concentrations of total cholesterol, triglyceride and LDL-cholesterol against an elevation of HDL-cholesterol levels compared to rats of hypercholesterolemia group. Furthermore we see that there's a significant difference ($p > 0.05$) results between the group treated with *Tanopati* and the other treated with Questran® regarding the concentrations of total cholesterol and LDL cholesterol, but no significant difference ($p > 0.05$) results in terms of triglyceride and HDL for both groups.

The link between dyslipidemia cardiovascular diseases is particularly well established. The elevation of Total Cholesterol and LDL Cholesterol is associated with an increased cardiovascular risk. A low concentration of HDL can be regarded as an additional risk factor, then a high concentration of the HDL is a protective factor. Because of this inverse relationship between cardiovascular risk and LDL one hand, the other hand HDL, it has been proposed that the ratio [total cholesterol/HDLC] or atherogenic index as preacher cardiovascular risk. Particularly cardiovascular risk increases when this ratio exceeds 5. Figure 36 shows the estimated cardiovascular risk of different groups. The results indicate that cardiovascular risk is very High significantly ($p < 0.05$) in the group of rats addicted to cholesterol compared to that of animals of normal control groups. Treatment with *Tanopati* and Qestran® extract significantly decreased ($p < 0.05$) this risk with values below normal for *Tanopati*.

b) Effect of Tanopati on blood pressure and heart rate in rabbits (BP and HR)

Table 1 shows the values of cardiovascular parameters systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) of animals of

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the control lots, sick not treated and treated with *Tanopati* and Tenordate® (atenolol+nifedipine).

Cardiovascular parameters values for animals in witness lot, SBP, DBP and HR were respectively 123.4±0.2 mmHg for SBP; 81.1±3 mmHg for DBP and 230.8±5.7 beat/min for HR. These values increased significantly ($p < 0.05$) after the induction of hypertension in rabbits respectively to 178.5±0.5 mmHg for SBP, 117.43±1.33 mmHg for DBP and 329; 97±2.3 beat/min for HR that is a percentages increase of 44, 65.43%, 44.79%, 42,96% respectively. These parameters (SBP, DBP and HR) decreased significantly ($p < 0.05$) up to their normalization with the treatment of Tenordate® (10 mg/kg bw) and *Tanopati*, at doses of 10 mg/kg bw. The SBP values change from 178.5±0.5 mmHg to 120.7±1.6 mmHg for SBP, 117.43±1.33 mmHg to 83±1.3 mmHg for DBP and 329; 97±2.3 mmHg to 231±1; 21 mmHg for after 14 days of treatment with *Tanopati*. With Tenordate® (10 mg/kg.bw), the values obtained are 117.84±0.7 mmHg, 79.61±2.1 mmHg and 223±4.5 mmHg for SBP, DBP and HR respectively.

Table 1: Values of SBP, DBP, and HR in rabbits treated and not treated with adrenaline, the Tenordate and *Tanopati* after 14 days of treatment.

Treatments	Cardiovascular parameters		
	SBP	DBP	HR
Distilled water	123.4± 0.2[a]	81.1± 3.0[a]	230.8± 5.7[a]
Adrénaline	178.5± 0.5[b]	117.43± 1.33[b]	329.97± 2.3[b]
Adrénaline+ *Tanopati*	120.7± 1.6[a]	83±1.3[a]	231± 1.21[a]
Adrénaline+ Ténordate®	117.8± 0.7[a]	79.61± 2.1[a]	223± 4.5[a]

Values are means±SEM for 4 rabbits. a and b are row values with different superscripts are significantly different ($p < 0.05$).

SBP: systolic blood pressure, DBP: diastolic blood pressure, HR heart rate.

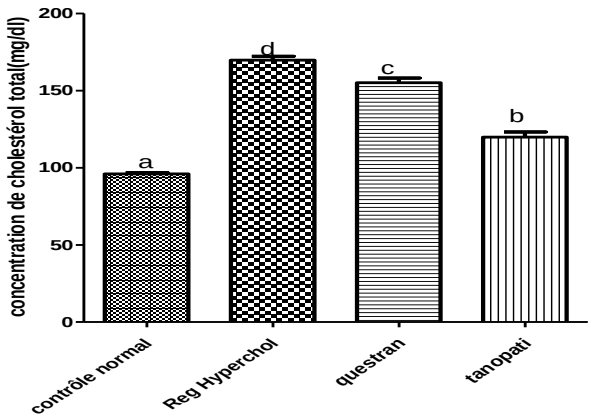


Figure 1: Effect of the extract of *Tanopati* on total cholesterol.

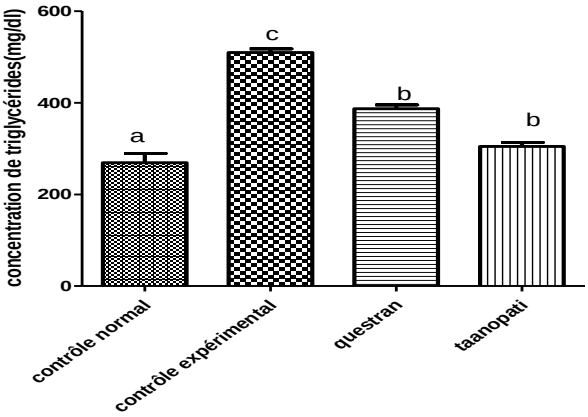


Figure 2: Effect of the extract of *Tanopati* on triglycerides.

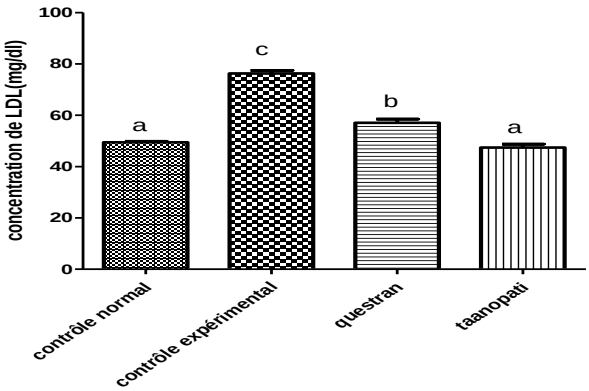


Figure 3: Effect of the extract of *Tanopati* on LDL.

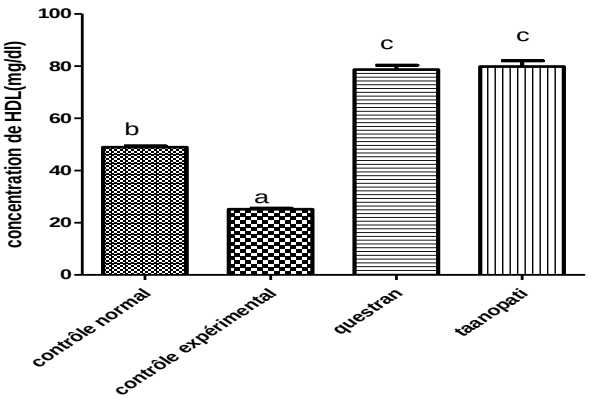


Figure 4: Effect of the extract of *Tanopati* on HDL.

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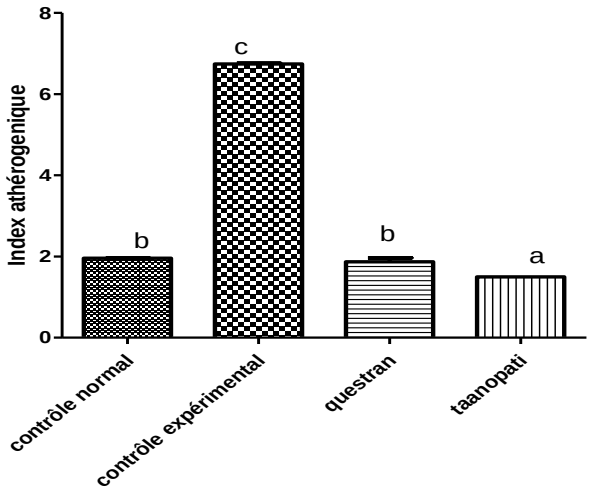


Figure 5: Effect of the extract of *Tanopati* on atherogenic index.

IV. Discussion

The results show that dietary cholesterol intake five times a week for six weeks in rats causes hypercholesterolemia resulted in an increase in total cholesterol, triglycerides and LDL cholesterol and decrease HDL cholesterol. In those circumstances, the lipids accumulate on the arterial wall, thereby forming a plate which occludes the lumen and reduces blood flow to vital organs such as the heart, brain, liver, or kidney. This narrowing of the vascular lumen would result in the elevation of blood pressure. The increase in the level of triglycerides, total cholesterol and LDL cholesterol and reduced HDL cholesterol thus promote the development of atherosclerosis and hypertension.[14]

Our results indicate that the extract of *Tanopati*, administered at the doses of 10 mg/kg bw causes a decrease of the concentrations of triglycerides, total cholesterol and rendered LDL serum cholesterol in rats hypercholesterolemic by consumption of dietary cholesterol. The underlying mechanism by which the extract *Tanopati* exercised its hypocholesterolemic effect may be a decrease in intestinal absorption of cholesterol by binding with the bile acids in the intestine and increased biliary excretion.[15]

Tanopati could also act by reducing cholesterol biosynthesis specifically by decreasing the activity of hydroxymethylglutaryl-coeenzyme A (HMG-CoA) reductase.[16] In addition, the *Tanopati* could lower the concentration of serum cholesterol by modifying the lipoprotein metabolism, enhancing the absorption of LDL by the LDL receptors increase and/or increasing the activity of lecithin acyl transferase-cholesterol (LCAT).[17]

The link between dyslipidemia and cardiovascular diseases is particularly well established. The elevation of Total Cholesterol and LDL Cholesterol is associated with an increased cardiovascular risk. A low concentration of HDL-C can be regarded as an additional risk factor, and then a high concentration of HDL-C is a protective factor. Because of this inverse relationship between cardiovascular risk and LDL one hand, the other hand HDL, it has been proposed to use the ratio [total cholesterol/HDL-C or atherogenic index as cardiovascular risk predictor. The cardiovascular risk increases particularly when this ratio exceeds 5 according to the Framingham study. Our results indicate a ratio of 6.7 in rats made hypercholestérmiques, meaning exposure to high risk of cardiovascular disease. However, the treatment with the *Tanopati* significantly reduced this index in hypercholesterolemic animals by passing 6.7±40.2 to 1.5.

This could still justify antihyper-cholestérolémique effect of the extract of *Tanopati*. According to Nwankpa et al, *Phyllanthus* sp has a protective role against cardiovascular disease by significantly reducing the serum total cholesterol, LDL, triacylglycerides and atherogenic index which is a predictor of risk factor, and by the significant increase in HDL.18 The presence of *Phyllanthus* sp, *Tanopati* in the recipe so to justify the low atherogenic index and antihypercholestérolémique effect observed.

Furthermore, the phytochemical screening extract *Tanopati* indicated that it contains flavonoids, tannins and saponin glycosides. Flavonoids and tannins play an important role in lipid metabolism. Flavonoids block specific enzymes. For example, flavonoids block converting enzyme (ACE), which increases blood pressure, cyclooxygenase (COX) and prostaglandin-endoperoxide synthase (PTGS), catalyze the formation of prostaglandins from arachidonic acid.19 Flavonoids also protect the vascular system and strengthen capillaries that carry oxygen and vital nutrients to all cells.[19] As tannins, they form complexes with proteins and make them unavailable for the cells.20 The significant increase in serum concentration of triglycerides observed may be due to the ability of tannins extract *Tanopati* to form complexes with the HMG CoA reductase inhibitor and cyclooxygenase. These tannins and prevent normal metabolism enzymes leading to lipid accumulation in the serum. Extract *Tanopati* thus improves the lipid profile in rats and reduces atherogenic risk.

Hypertension was induced in rabbits after 14 days of daily treatment with adrenalin. This hypertension would settle according to various molecular mechanisms'. I) At the heart, the link coupled with the G protein (Gs) to β1 receptors leads to activate adenylyl cyclase (AC), which converts ATP into cAMP. The cAMP activate protein kinase A (PK-A) which in the turn allows phosphorylation of the calcic channels thus involving the increase the flow of the calcium from endoplasmic reticulum. It follows from there an increase in the force (positive inotropic effect) and the frequency (positive chronotropic effect) of the heart. This increase in force and frequency of the heart then cause elevation of blood pressure.[21] (ii) The adrenaline in the blood vessels

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directly activates natriuretic peptide and vasopressin which activate the calcium channels in the endothelium causing the release of calcium and increased calcium flow as a result of vasoconstriction leads to the elevation of blood pressure.[22] (iii) The adrenaline binds to the β-adrenergic receptor present on the juxtaglomerular kidney unit to activate adenylyl cyclase (AC), which converts ATP into cAMP. The cMPA activates protein kinase A which involves the release of renin. Renin converts angiotensin I to angiotensin II, leading to vasoconstriction and thus high blood pressure.[23]

In this study, the results show that the extract of *Tanopati* normalizes in eight days cardiovascular parameters namely systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) of hypertensive animals. The phytochemical screening showed that the extract *Tanopati* is rich in polyphenol, while according to Lorenz et al.[24] polyphenols act by rapid dose-dependent and sustained activation of the PI3K/PKB (phosphatidylinositol 3-kinase/protein kinase B) pathway which phosphorylates the endothelial nitric oxide synthase (eNOS). This phosphorylation occurs on serine 1197 independently of the intracellular Ca^{2+} and activation of eNOS in response to the increase in intracellular Ca^{2+} via the Ca^{2+} complex-CAM (calciumcalmodulin).[24] The production of NOS would thus involve a vasodilation and consequently a normalization of cardiovascular parameters.

The vasodilator and vasculoprotective effect of polyphenols is potentiated by amplification of the effectiveness of endogenous antioxidants, like catalase, inhibition of the pro-oxidant enzymes (NADPH oxidase) and the dismutation of the surrounding ROS. We used Ténordate® as an antihypertensor of reference because Ténordate® is an association of atenolol and nifedipine. Our results show that the extract of *Tanopati* has the same effects as Ténordate®, it could thus act by its mechanism.

Indeed, Nifedipine is a calcium antagonist and atenolol, a β blocker. Ténordate® acts by inhibiting the calcium channel, preventing the entry of calcium into the contractile structures, thus causing the decrease in cardiovascular parameters or by binding to adrenergic β receptors, consequently preventing the release of calcium into the intracellular environment. This results in vasodilation and a decrease in systolic blood pressure, diastolic blood pressure and heart rate.25 The extract of *Tanopati* could therefore contain antagonist compounds of calcium and/or β blockers.

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NT-proBNP as a Diagnostic Marker in CCF

By Dr. Hitesh M R & Dr. Vedavathi R
Kempegowda Institute of Medical Sciences, Bangalore

Introduction-

- Heart failure prevalence is raising throughout the world.
- The overall prevalence of HF is thought to be increasing because current therapies for cardiac disorders, such as Myocardial Infarction (MI), Valvular Heart Disease, and Arrhythmias, are allowing patients to survive longer.
- American Heart Association (AHA) guidelines define HF as a "Complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood, which in turn leads to the cardinal clinical symptoms of dyspnea and fatigue and signs of HF namely edema and rales".
- Making the correct diagnosis in patients with Suspected Acute Heart Failure is challenging, and confirmatory in only 40-50% of Cases.
- Several Studies have shown that when added to routine history, Clinical Examination and Conventional investigations measurement of plasma natriuretic peptide levels improve diagnostic accuracy.
- B-type natriuretic peptides (BNP) that are synthesized by the left and right atria in response to cardiomyocyte stretching.
- The human BNP gene encodes a 108 amino acid pro hormone named proBNP.

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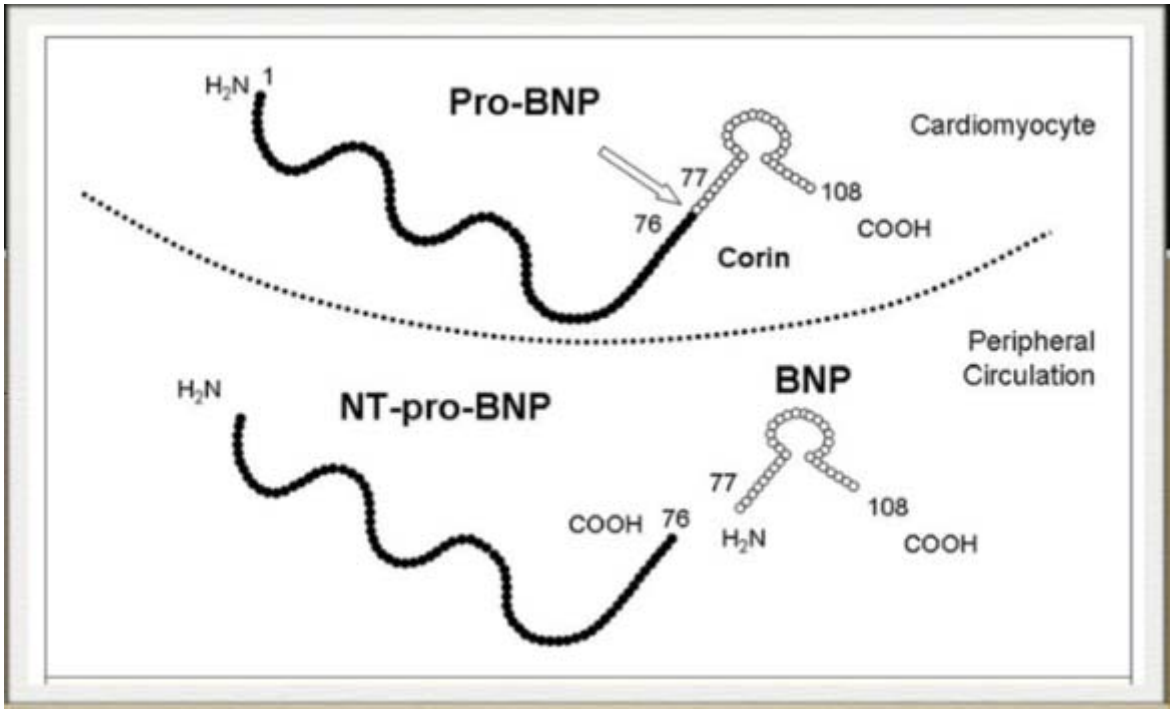
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NT-proBNP as a Diagnostic Marker in CCF

Dr. Hitesh M R [α] & Dr. Vedavathi R [σ]

I. Introduction

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- B-type natriuretic peptides (BNP) that are synthesized by the left and right atria in response to cardiomyocyte stretching.
- The human BNP gene encodes a 108 amino acid pro hormone named proBNP.
- ProBNP is cleaved in to a biologically active 32-amino acid C-Terminal polypeptide (BNP) and a 76-amino acid N-terminal fragment termed NT-proBNP.
- Both these polypeptides are released in to the circulation and can be detected in blood samples.

II. Materials and Methods

- The study was conducted on 60 patients between the age group of 40-70 years attending the inpatient and outpatient clinic at Kempegowda Institute of Medical Sciences, Bangalore.
- It was a case control comparative study of 60 patients (30 cases and 30 controls) during the study period from November 2013 to October 2015.
- Informed consent was obtained from all patients /care takers of the patients enrolled for the study.
- The data of the patients was collected in a well designed platform.
- Relevant data about diabetes mellitus, hypertension and Renal disease was taken in the history.

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- CBC, Urine Microscopy, RFT, LFT, RBS, Serum Electrolytes, Lipid profile, ECG, Chest X-RAY and 2D Echocardiography was done for all patients.
- Serum NT-proBNP levels were measured by ELFA (Enzyme linked fluorescence Assay) technique.
- STASTICAL ANALYSIS: Unpaired t test and chi-square test.
- *CASES:* Patients suspected to have heart failure based on history, Clinical examination and ECG (Age and Sex Matched individuals).
- *CONTROLS:* Patients without heart failure and diseases mentioned in Exclusion Criteria.
- In our study cutoff levels for NT-pro BNP was
  1. >450 pg/ml for those aged < 50 years.
  2. >900 pg/ml for those aged 50-70 years.

a) Inclusion Criteria

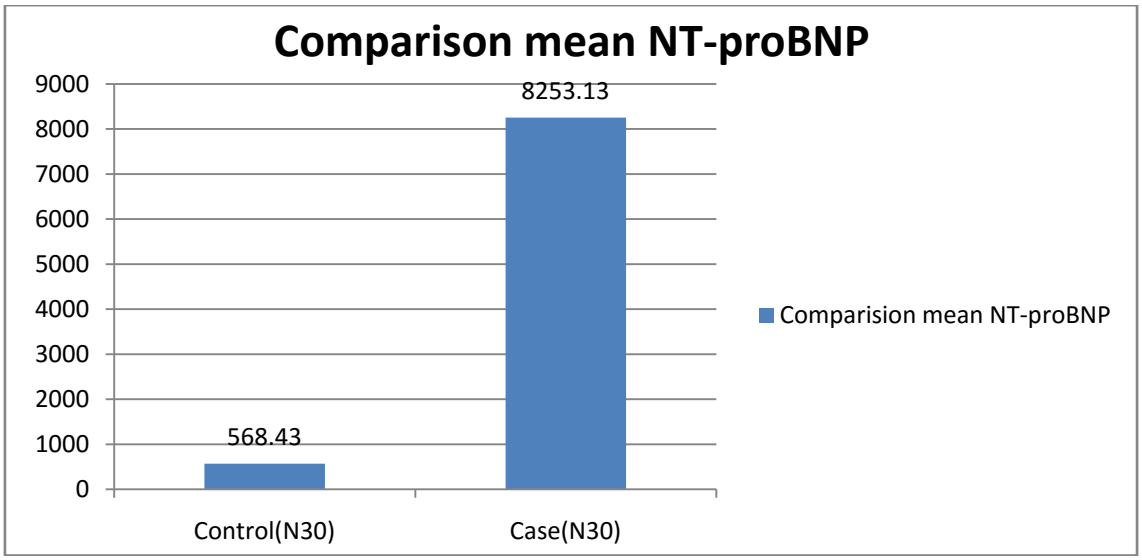
1. Age 40-70 years.
2. Complains of sudden onset dyspnea suspected to be due to cardiac causes.
3. Patients who signed the written informed consent.
4. Patients who did not meet the exclusion criteria.

b) Exclusion Criteria

1. Cor pulmonale.
2. Sepsis.
3. Lung Cancer.
4. Pulmonary Embolism.
5. ARDS.
6. Liver Cirrhosis.
7. Renal failure.
8. Patients not willing to participate in the study.

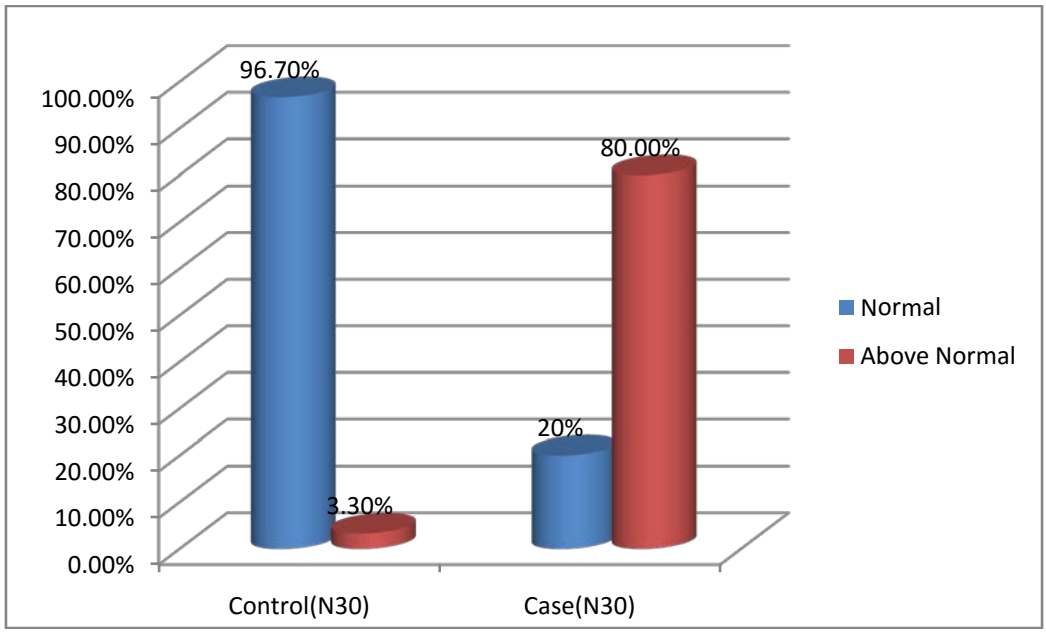
III. Results

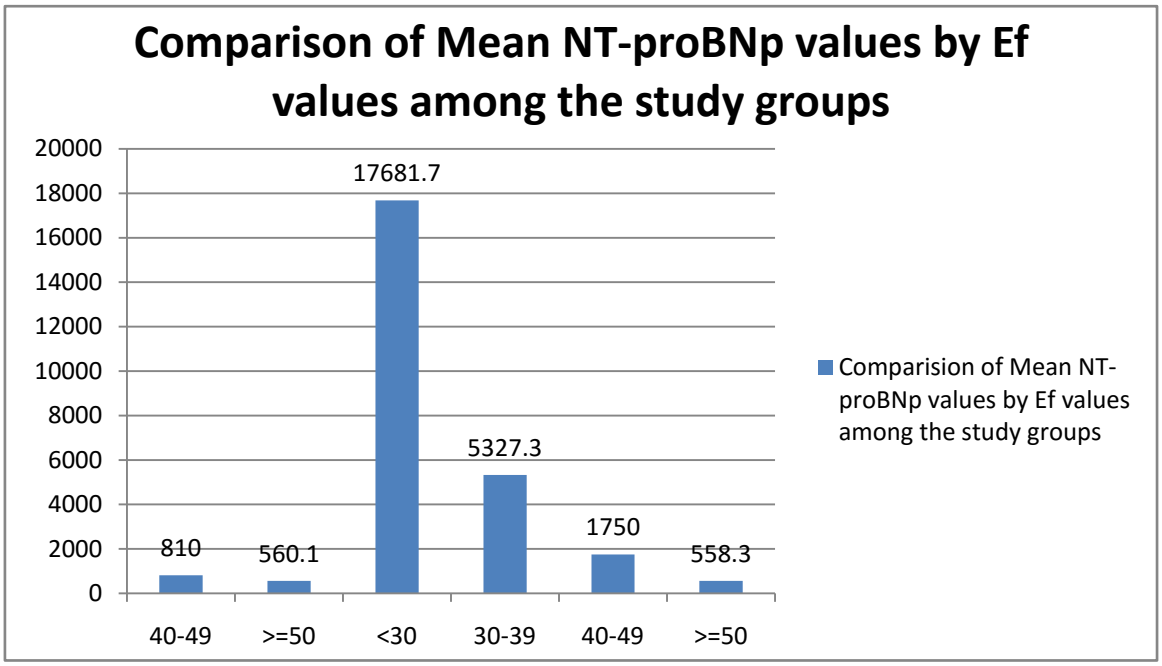
Comparison of mean NT-proBNP:



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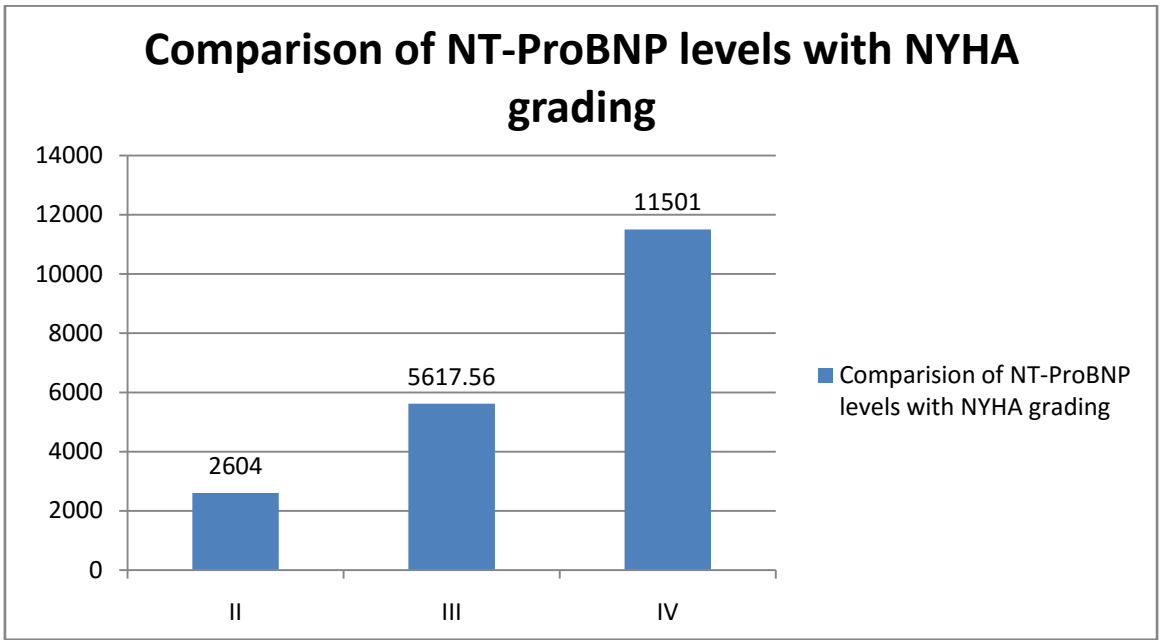
Comparison of NT-proBNP among cases and controls:



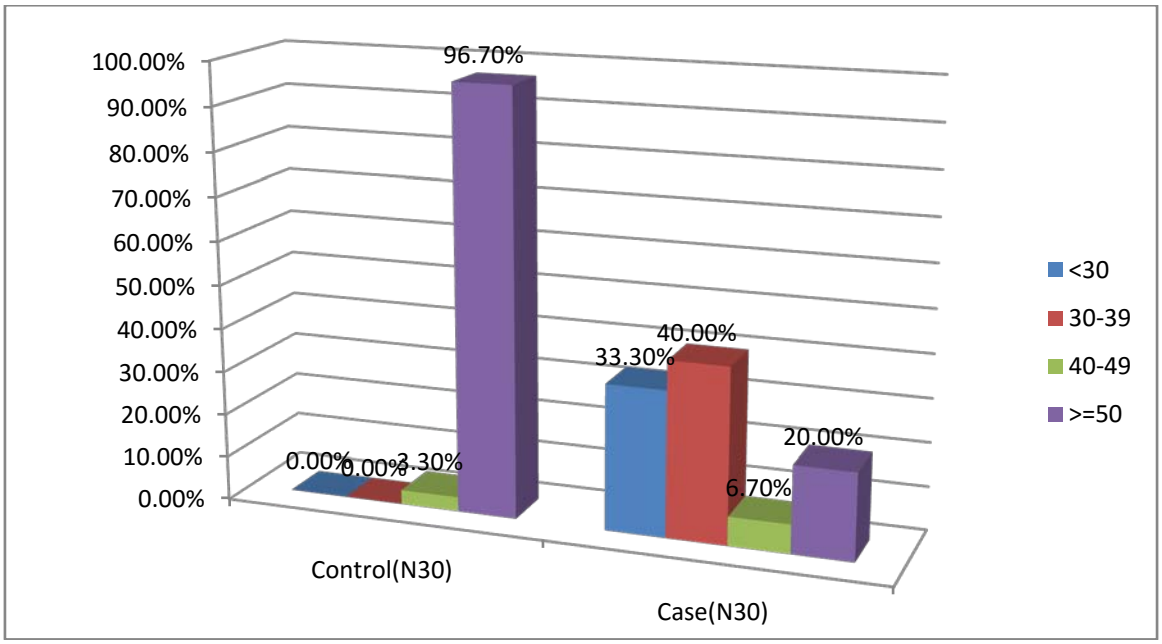


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Comparison of NT-proBNP levels with NYHA grading:

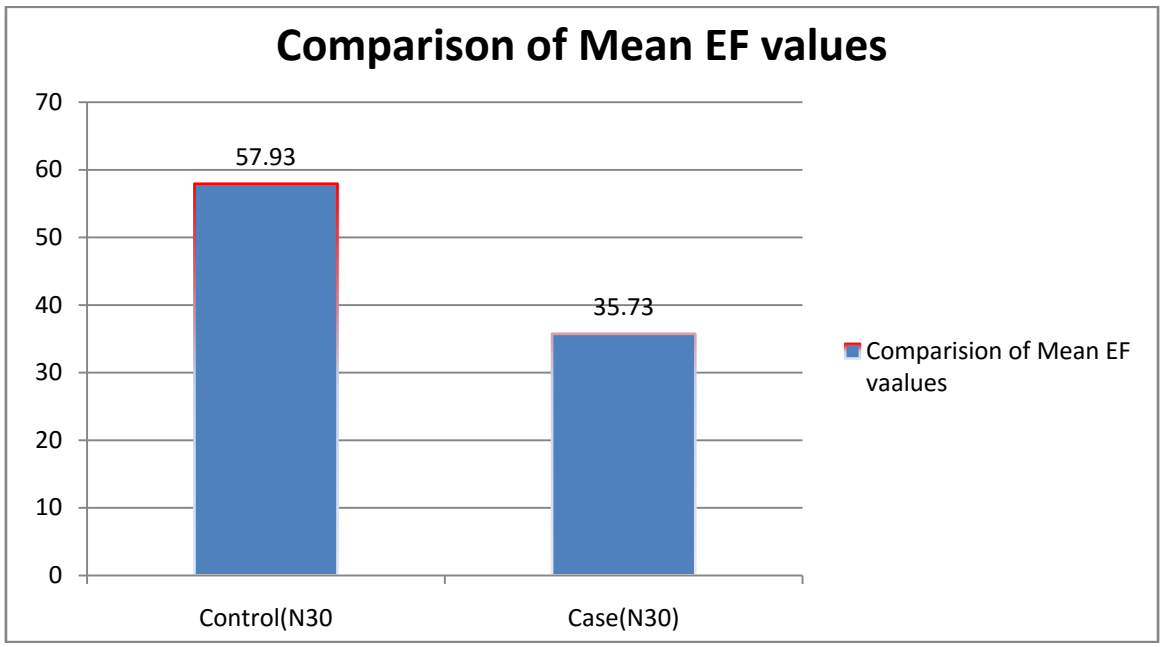


Comparison of EF Values:

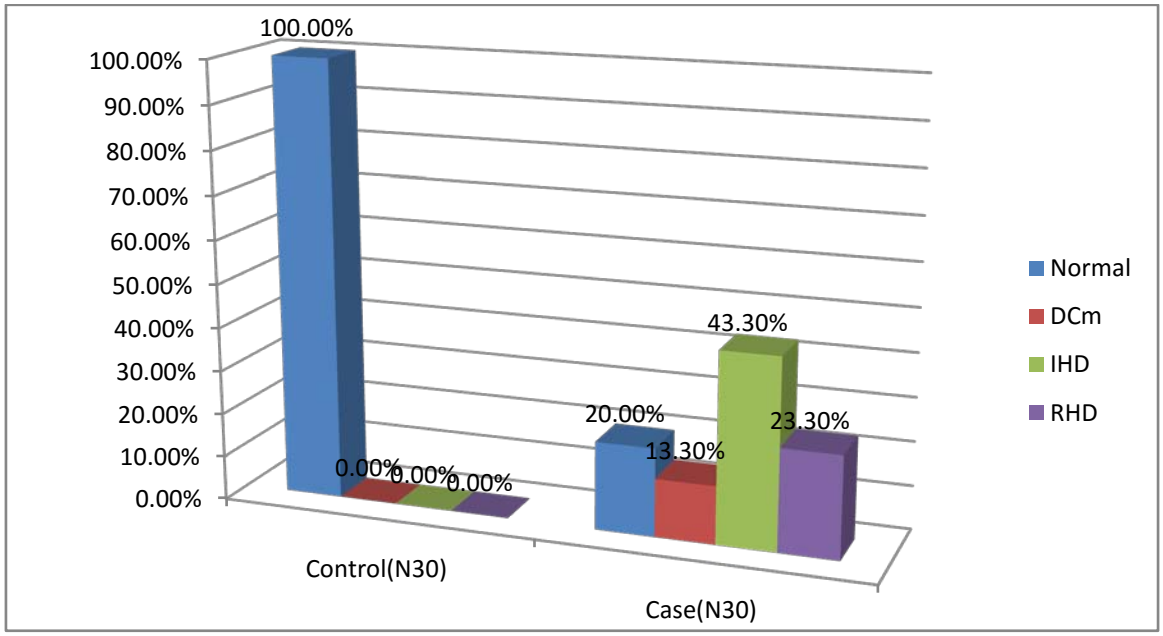


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Comparison of Mean EF Values:



2D-Echocardiography Report Comparison:



IV. Discussion

- Among 30 controls:

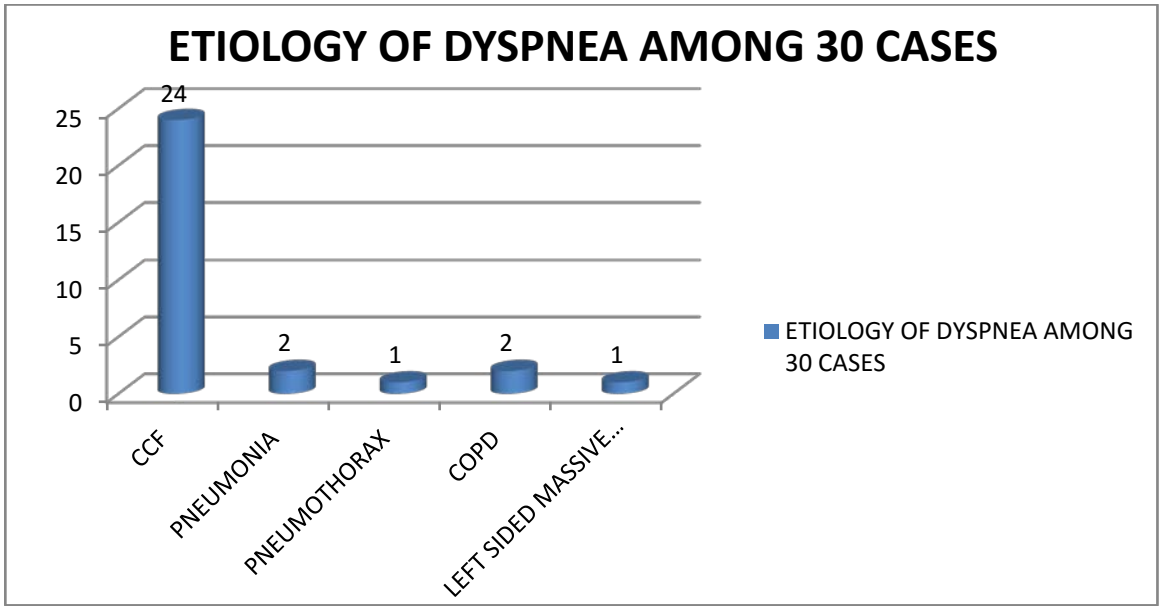
1. 29 had NT-proBNP levels within normal range for their age.
2. 1 had elevated level of NT-ProBNP for their age.

- Among 30 cases:

3. 24 had NT-ProBNP level elevated for their age and were diagnosed to have congestive cardiac failure.
4. 6 had NT-ProBNP levels within normal limits for their age. These 6 patients had a normal 2D-ECHO. Breathlessness in these patients was due to non cardiac cause.

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Etiology of Dyspnea among 30 Cases:



V. Discussion

- The mean value of NT-proBNP raises with decreasing EF. NT-ProBNP values have a inverse relationship with Ef Values. There was a strong correlation between the 2 variable with a p value of <0.001
- There is a raise in NT-proBNP value with increasing NYHA grades. There was a significant correlation between the 2 variables with a 'P' value of 0.049
- The mean NT-ProBNP Value among controls was 568.43 pg/ml. The mean NT-proBNP value among cases as 8253.13pg/ml. It was statistically significant with a 'P' value of <0.001.

VI. Conclusion

1. Serum NT-proBNP levels are significantly elevated in cases compared to controls making it a valuable diagnostic marker in Congestive Cardiac Failure.
2. Serum NT-proBNP levels correlative inversely with the EF levels.

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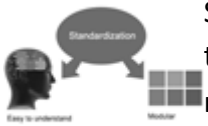


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Content

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- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
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- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
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- Manuscript should complement any figures or tables, not duplicate the identical information.
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Approach

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- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
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- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

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References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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