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Pharma, Drug Discovery, Toxicology & Medicine

Effect of Drug Abuse on Youths

Research of Pharmacological Activity

Highlights

Dry Extract from Echinacea Purpurea

Oxidative Stress and Diabetes Mellitus

Discovering Thoughts, Inventing Future

VOLUME 22 ISSUE 1 VERSION 1.0

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The Effect of Drug Abuse on Youths in Portloko Town, Northern Sierra Leone

By Sylvia Kercher Bangura & Ijatu Sesay
Ernest Bai Koroma University of Science and Technology

Abstract- Drug abuse and addiction have been part of youths in this part of the community in their existing social systems, affecting crime rates, hospitalizations, child abuse, and child neglect, frustration, insane, and disability, HIV /AIDS, Scabies and skin diseases, anaemia, pale in colour. those who take intra venous injections suffer from HIV/aids. Youth nowadays try various drugs so that they feel different from normal, Drugs has become a fashion amongst youth nowadays, both boys and girls are greatly involved in this habit. This paper is presenting the results of the causes, types, effects on the individuals, families, and community as a whole. The different types of drugs taken by youth in these communities were tramadol, pampas, Evostick-, super glue, marijuana, tobacco, pounded tobacco with bicarbonate of soda (snuff), cocaine, petrol, Araldite, kola nut, and alcohol. The factors that lead to the intake of these drugs are as follows, unemployment, lack of effective mentorship, lack of family values, poor parenting guidance, and loss of hope easily assessable, and affordable, peer group influence, cults, secret societies in contributed to youths going into drug This study.

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The Effect of Drug Abuse on Youths in Portloko Town, Northern Sierra Leone

Sylvia Kercher Bangura [α] & Ijatu Sesay [σ]

Abstract- Drug abuse and addiction have been part of youths in this part of the community in their existing social systems, affecting crime rates, hospitalizations, child abuse, and child neglect, frustration, insane, and disability, HIV /AIDS, Scabies and skin diseases, anaemia, pale in colour. those who take intra venous injections suffer from HIV/aids. Youth nowadays try various drugs so that they feel different from normal, Drugs has become a fashion amongst youth nowadays, both boys and girls are greatly involved in this habit. This paper is presenting the results of the causes, types, effects on the individuals, families, and community as a whole. The different types of drugs taken by youth in these communities were tramadol, pampas, Evostick-, super glue, marijuana, tobacco, pounded tobacco with bicarbonate of soda (snuff), cocaine, petrol, Araldite, kola nut, and alcohol. The factors that lead to the intake of these drugs are as follows, unemployment, lack of effective mentorship, lack of family values, poor parenting guidance, and loss of hope easily assessable, and affordable, peer group influence, cults, secret societies in contributed to youths going into drug This study. The main objective of this study was to investigate the causes and effects of drug abuse on the youths in portloko township, forty (40) participants were investigated in this study, thirty (30) youths and ten (10) young adults /adults, the investigation focused on the different types, causes and effect of the abuse of these drugs Questionnaire was analysed statistically using tables, frequencies, and percentages, while qualitative data from the interview was analysed and presented recommendations were made on how to minimize or prevent our youths from drugs, the conclusion was made on the cause and prevention of these drugs taken by youths in these community.

I. Introduction

A *drug* is any chemical substance that causes a change in an organism's physiology or psychology when consumed, Drug abuse is defined herein as illicit production, trafficking, and consumption.

Drug abuse can affect several aspects of a person's physical and psychological health. Certain drugs *can lead to drowsiness and slow breathing*, while others may cause insomnia, paranoia, or hallucinations. Chronic drug use is associated with cardiovascular, kidney, and liver disease.

Drug addiction is one of the major problems in this community. Since these communities have young populations, they are at greater risks of addiction. The young population is exposed to higher risk as a major and the most vulnerable group. Problems of puberty, adolescents and youth identity crisis, and mental conditions can be considered as important factors for the tendency of this age group towards addiction (Petraitis J, Flay BR, Miller 2011). The use of drugs in adolescents who their friends have a positive attitude towards drugs is higher, even up to two-thirds of the causes for using the drugs is how much close friends talk about the drugs, and a friend suggests them to accept the use of drugs Petraitis J, Flay BR, Miller 2019) As well as pleasure, curiosity and escape of from home. Addiction has engaged all industrial and nonindustrial societies along with malnutrition and environmental pollution; so that addiction had a growing trend during the recent years in Sierra Leone (Heidari H, Sharif Malmir M 2013). close friends talk about the drugs, and a friend suggests them to accept the use of drugs (Ghoreishi Zadeh SMA 2001) As well as pleasure, curiosity, and escape of psycho-social problems are the major causes of early drug use for the first time Ghoreishi Zadeh SMA 2002).

Heidari et al. concluded that low self-esteem, successive failures in life, and observational learning from addicted family members were the most common causes of a tendency towards drugs (Heidari H, Sharif Malmir M 2013). Yuki Maehara et al. investigated the factors influencing relapse of drug usage in Bangladesh during 5 months after drug withdrawal and concluded that the relapse rate is higher in women. In the male population, the most common factors influencing relapse included unstable housing, living alone, and high income. In the female population, the most common factors of relapse included having no child for emotional support and working as a sex worker (Maehira Y, Chowdhury EI 2013) Mir Lotfi et al. evaluated the attitudes of students in the dormitory of Zahedan City towards the drug abuse and they concluded that there are different causes for a tendency towards the drugs while staying in a dormitory is one of the most critical periods in people's lives and necessary and appropriate measures should be performed to solve social and mental problems in this period (Mir Lotfi P, Javadimehr 2015) Kilpatrick et al. also reported that the age of first use is obviously related to the future consumption patterns. As the drug usage is started sooner, it is correlated with the greater and more widespread use of other drugs (Kilpatrick DG, Acierno R 2013.

Author α: Faculty of Education, Ernest Bai Koroma University of Science and Technology. e-mail: sylviakercherbangura@gmail.com
Author σ: Faculty of Agriculture, Ernest Bai Koroma University of Science and Technology.

Illegal drugs are define as chemical formulas, but underground chemist can modify the molecular structure of certain illegal drugs to produce analogy known as designer drugs, which do not meet these definitions,, these drugs can several be stronger than the drugs they are designed to imitate

- Marijuana remains the most commonly used illegal drug: Approximately 80 percent of current illicit drug users are marijuana or hashish users. ...
- Cocaine Use. ...
- Heroin Use. ...
- Methamphetamine Use. ...
- Nicotine Use (Cigarettes and Smokeless Tobacco)...
- Inhalant Use. ...
- Hallucinogen Use. ...
- Anabolic Steroid Use

Drug abuse may lead to social, physical, emotional, and job-related problems.

Marijuana

It's still the most-used illegal drug in Sierra Leone., despite it recently earning legal status for medical purposes in many countries.

Marijuana refers to the dried leaves, flowers, stems, and seeds of the hemp (*Cannabis sativa*) plant, all parts of it can be used Most people smoke marijuana, but it can also be added to foods and eaten.

It can act as both a stimulant and a depressant, and even a hallucinogen.

Marijuana contains the chemical which acts on different parts of the brain to create the "high" that users experience, such as changes in sensations, mood, body movements, thinking, and memory.

When used regularly, marijuana can affect brain development and lead to cognitive problems. It can become addictive for some people, and also cause serious health problems such as breathing problems, increased heart rate, palpitation and a higher risk of heartattacks, depression, anxiety, and suicidal thoughts for some people. Among young people, heavy Marijuana use has been associated with cognitive impairment and mental illness, like schizophrenia. However, in adults, chronic use of marijuana has been associated with serious medical conditions.

Inhalants

Inhalants are mood-altering substances that are voluntarily inhaled. Most substances used are commercial and household products, such as solvents and aerosols, which are easily obtained and are not harmful, if used for the purpose intended and as directed. Because they are common products, inhalants often are a young person's first attempt at "getting high". Inhalants can severely impair judgment and driving ability. They also cause severe disorientation, visual distortion and confusion. There is evidence that tolerance to the effects of inhalants develops with continued use so, users need to increase use to obtain the same high. Studies have shown that dependence on inhalants continues even when the user goes on to use other drugs. Inhalants include: Nitrous Oxide, laughing gas, propellant aerosol cans, Amyl Nitrite, poppers, snappers in ampules, Butyl Nitrite, rush, bullet, climax (Kilpatrick 2018).

II. Stimulants

Stimulants are drugs that stimulate the central nervous system and excite bodily activity. Methamphetamine is one of the fastest-growing drugs of abuse. These drugs create less intense and less expensive cocaine-like effects in the body.

Persons who use large amounts of amphetamines over a long period of time can develop an amphetamine psychosis that includes hallucinations, delusions, and paranoia. These symptoms usually disappear when drug use ceases.

Amphetamines can be swallowed in pills or capsules, smoked as "crank" and "ice" or injected. An amphetamine injection creates a sudden increase in blood pressure that can result in stroke, very high fever or heart failure Stimulants are drugs that stimulate the central nervous system and excite bodily activity abuse.

Signs and Symptoms

Mood changes, Impaired concentration, Impaired mental functioning, Mood swings between apathy and alertness, Restless. Anxious and moody behaviour Increased heart and respiratory rates, High blood pressure, Profuse sweating, Loss of appetite Dizziness Blurred vision, Anxiety and sleeplessness.

A depressant is a drug that depresses the central nervous system, resulting in sedation and a decrease in bodily activity. Depressants, taken as prescribed by physicians, can be beneficial for the relief of anxiety, irritability, stress and tension. The main classes of medical depressants are barbiturates and benzodiazepines. When regular users suddenly stop taking large doses, they can develop withdrawal symptoms ranging from restlessness, insomnia and anxiety to convulsions and death. Babies born to mothers who abuse depressants during pregnancy may be physically dependent on the drugs and show withdrawal symptoms shortly after they are born. Birth defects and behavioural problems also may result. Depressants are known as S barbiturates, downers, and tranquillizers, such as Valium, Librium, Equanil, Serax, Tranxene, and Xanax.

The effect of depressants are in many ways similar to the effect of alcohol. small amounts can produce calmness and relaxed muscles .but somewhat larger doses can cause slurred speech.

Hallucinogens

Hallucinogenic drugs distort the senses and often produce hallucinations–experiences that depart

from reality. Some negative health effects may last six months to a year following prolonged daily use. Phencyclidine (PCP) interrupts the function of the neocortex, the section of the brain that controls the intellect and keeps instincts in check because the drug blocks pain receptors. Violent PCP episodes may result in self-inflicted injuries. Lysergic acid (LSD), mescaline, and psilocybin also are hallucinogens that cause illusions and hallucinations. It is common to have a bad psychological reaction to LSD, mescaline, and psilocybin. The user may experience panic, confusion, suspicion, anxiety and loss of control. Delayed effects or flashbacks can occur even after use has ceased.

Signs and Symptoms

Impaired concentration, Confusion and agitation, Muscles rigidity, Profuse sweating, A sense of distance and estrangement, Muscular coordination, Blocked and incoherent speech, Dilated pupils Health Effect, Raised in body temperature, Increased heart rate and blood pressure, Loss of appetite, Sleeplessness, Tremors, Frequent memory loss, Speech difficulties, Change of mood such as depression' anxiety and violent behaviour, Hallucination, Convulsion and coma, Heart and lung failure.

Narcotic analgesics are the most effective compounds used for pain relief. Narcotic analgesics include Opium, Opiates (morphine, codeine, Percodan, heroin, and Dilaudid), and Opioids (synthetic substitutes such as Vicodin, Darvon, Demerol, and methadone). Narcotics can be smoked or eaten (opium), injected, taken orally or smoked (morphine), inhaled, injected, or smoked (heroin). Opiates also are known as heroin, smack, horse, brown sugar, and black tar.

Designer drugs are also related to amphetamines and have a mild stimulant property but are mostly euphoriants. They can cause brain damage and can produce symptoms such as severe Parkinson's disease. paralysis and irreversible brain damage, nausea and vomiting. impaired speech. Chill's faintness, shock and blurred vision 'impaired perception, illusion

Signs and Symptoms

Drowsiness Nausea and vomiting, Constricted pupils, Watery eyes and itching, Low and shallow breathing, Cold and clammy skin, Difficulty in breathing, Tramadol is *a strong painkiller.* It's used to treat moderate to severe pain, for example after an operation or a serious injury. It's also used to treat long-standing pain when weaker painkillers no longer work. It also has side effect tramadol can slow or stop breathing, and may be habit-forming, misuse of drugs can lead to *addiction and over dose can lead to death.*

Sleepiness. headache. Nervousness. Uncontrollable shaking of a part of, the body. Muscle tightness. Changes in mood. heartburn or indigestion. Dry mouth.

Alcohol

drink, booze, liquor, beverage, bevvy, plonk, vino

Alcohol (chemical name *ethanol*) is usually found as a beverage and is a colourless liquid in its pure form.

It acts by slowing down the body's reactions in many different ways.

There are three main forms of alcoholic drink, divided by strength:

- Beers - up to 7-8% ABV (alcohol by volume)
- Wines - up to 20% ABV
- Spirits - up to 40% ABV (in the UK)

ABV: Alcohol by volume (abbreviated as ABV, abv, or alc/vol) is a standard measure of how much alcohol (ethanol) is contained in an alcoholic beverage (Mir Lotfi P, Javadimehr M, 2015)

Inhalants

- Inhalants are mood-altering substances that are voluntarily inhaled. Most substances used are commercial and household products, such as solvents and aerosols, which are easily obtained and are not harmful, if used for the purpose intended and as directed. Because they are common products, inhalants often are a young person's first attempt at "getting high". Inhalants can severely impair judgment and driving ability. They also cause severe disorientation, visual distortion and confusion. There is evidence that tolerance to the effects of inhalants develops with continued use so, users need to increase use to obtain the same high. Inhalants include: Nitrous Oxide, laughing gas, propellant aerosol cans, aerosol sprays, aerosol paint cans, containers of cleaning fluid, ((Hojati H, Alvestany (2020) parental divorce or high genetic susceptibility is the main causes of addiction in the high risk youth Sundquist K,) Heidari et al.(2019).

III. Aims and Objectives

a) Aims

The aim of the study is to investigate the effect of drugs on the youth of Port Loko township.

b) The Objectives of the Study are Follows

1. To find out reasons why youth take drugs
2. To identify the types of Drugs taken by youths
3. To find out the different route of Administration
4. to find out the effect of drugs on; 1 self 11 Home 111 community/Nation
5. To find solutions and recommendation on how to minimize, rehabilitate and prevent the use of illegal drugs

c) Research Questions

What are the reasons why youth take drugs?

List the different type of drugs taken

What are the route of taken these drugs?

What are the e effect of these drugs on 1 oneself, 2 families 3 community/ Nation?

d) Statement of the Problem

Drugs have become the order of the day in port loko township, most youth are invlove in the taken of drugs, as they believe that it is part of their diet, drug addiction is so peculiar amongst them as there are a lot of hidden places that are known to them that are in the habit of selling drugs at affordable price, and it can be assessable and affordable most drugs are not bought with pricription, so can easily buy tranqulizers and sedatives and pain releiving drugs at any pharmacist or drug stores to quench there desires, even thogh these drugs stores are monitored by bphamacist board they sell behind counters, and because these youths been addicted with drugs, most of them are found in the street mad, insane, frustrated, thieves, gamblers, prostitude, teenage pregnancy, infections like HIV/AIDS. hapatitis .pneumonia, tuberculosis. cough, anaemia, fisto vagina futularchild mother and suicidal etc, all these have incure a lot on the Government and community in building rehabilitation centres, recruitment of staffs, and medicines, unrest on the part of the communit and drop out etc.

IV. Method of Data Presentation and Analysis

The quantifiable data from the questionnaire was analysed statistically using tables with frequencies and percentages while the qualitative data from the interview was analysed qualitatively using simple description or narration. That is data collected from the interview and questionnaire were presented and analysed separately. The raw data directly collected by the researcher from sources such as questionnaire, oral interview, observation and case study. Questionnaire and person-to-person interview were the primary sources of data collection in this study. Journals, the internet and newspapers, especially those that have important information pertaining the uses and effect of drugs were also of great used in this sturdy.

V. Sample Size and Sampling Techniques

The sample was selected randomly and purposively. The random technique gave every member equal opportunity and was used to guide the selection of appropriate samples to ensure that generalization of sample finding are representative of the population. The other technique used was purposive sampling as Bryman, (2008) pointed out that it is used to select subjects based on their relationship with the research questions. This technique was employed to identify key respondents in the various categories of people in the study area.

Considering the gender sensitivity, gender equality and equity aspects implicated in the study equal numbers of male (20) and Female (20) respondents were selected- which give a total of forty (40) persons interviewed. Amongst these were ten (10) adults (5) five women and five (5) men and thirty (30) youths and young adults.

VI. Results. Discussion and Analysis

Table 1: Responded Interviewed and Age Bracket

SEX	AGE IN YEARS					
	12-19 YRS		20-28 YRS		30 yrs and Above	
	No	%	No	%	No	%
MALE	10	25	5	12..5	5	12.5
FEMALE	8	20	7	17.5	5	12.5
TOTAL	18	45	12	30	10	25

The table above explain the sex and ages of those interviewed, there are a total of twenty (20) males and twenty (20) female, 25% of males are within the ages of 12-19 years,12.5% 20-28 years,12.5% .30 years and above female 20% within the ages 12-19 years .17.5% 20-28 years,12.5% 30 years and above'

Figure 1: Reasons Why People Take Drugs

- **Emotional:** Feeling they need drugs to fill a void in their lives (whether it's stress, trauma, relationship issues or more)
- **Physical:** Feeling like they need the physical effects of a high or low to physically feel better
- **Psychological:** General feelings of inadequacy towards themselves or the world, so they use drugs to boost their confidence and self-esteem

To fit in to society, one finds himself. To feel good, to experiment Availability of drugs, Grieving a death end of a relationship, Mental illness, Environmental influences. Relaxation, Self-medication. Financial burdens. Career pressure School pressures, Family demands, Peer and Social Pressure Abuse and trauma, Boredom, to fit in, Curiosity and experimentation, Rebellion to be in control. To enhance performance, solation Misinformation or ignorance, Instant Gratification, Wide availability, actors such as unemployment, lack of effective mentorship, lack of family values, poor parenting guidance, and loss of hopes.

Table 2: Different Types of Drugs route of Administration and its effect on Youths and Young Adults in the Port Loko

Drugs	Route of Administration	Effects
Alcohol	Oral mouth	• Salivary gland damage. • Gum disease and tooth decay. • Oesophageal ulcers. • Acid reflux and heartburn. • Stomach ulcers and gastritis. • Internal bleeding • alcohol **interferes with the brain's communication pathway** • change mood and behaviour, and make it harder to think clearly and move with coordination. Haemorrhoids
Tramadol	Oral mouth	**Nausea, vomiting, constipation, light-headedness, dizziness, drowsiness, or headache**
Cocaine	Inhalation	
Marijuana	Smoking	
Sanitary pad (pampas)	Boil with or without milk	Dizziness, weakness ,fatigue nausea, vomiting
Kush	Smoking	Weakness .fatigue. .sleeps a lot, nervousness, increased energy, increased appititie. hyper reactive ▪ Rapid heart rate ▪ Excessive worrying ▪ Sweating ▪ An impending sense of doom ▪ Mood swings ▪ Restlessness and agitation ▪ Tension ▪ Insomnia
Kolanut	Oral mouth,	Nervousness. loss aplite, palpitation, increased heartbeat,
Ataya	Drinking	Hyperactive, nervousness, increases appetite, increase heartbeat, palpitation,
Evostick	Inhalation	Drowsiness, dizziness, drowsiness weakness
Tobacco	Smoking	Palpitation, hyperactive, dizziness
Aridite	Inhalation	Hyperactive, dizziness, palpitation,
petrol/paint	Inhalation	Dizziness. palpitation, heartbeat, weakness.
Super glue /bleach/aerosol can	Inhalation	Dizziness. weakness. heartbeat drowsiness hyperactive
Snuff (Pounded tobacco mix with bicarbonate of soda)	Underneath the tongue	Black and decay teeth, coughing. sneezing, palpitation. Drowsiness

Figure III

The Effect of Drugs on the individual

Drug abuse is one of the *risk than nonusers for mental health problems amongst youths,* including depression, conduct problems, personality disorders, suicidal thoughts, attempted suicide, and suicide academic declining grades, absenteeism from school and other activities potential of dropping out of school substance abuse. low level of commitment to education and higher truancy rates. Cognitive and behavioural difficulties other activities potential of dropping out reined by alcohol- and drug-using youth may interfere with their academic performance Injuries due to accidents (such as car motorbike, accidents), physical disabilities, abuse. Disproportionate Disorders that affect the decision, health-related problems (cough, human lack of motivation Sleep Disturbances Irritability Weight gain or loss Rapid heart rate, Excessive worrying. Sweating, an impending sense of doom, Mood swings, Restlessness and agitation Tension Insomnia other activities potential of dropping out of school substance abuse. low level of commitment to education and idents (such as carmotorbike, accidents), physical disabilities, abuse. Disproportionate Disorders that affect decision-making. Heart disease includes high blood pressure, Psychosis, Reduced immune function, Stomach issues, Respiratory problems Liver Damage Kidney diseases, teenage pregnancy, child-mother, visto vagina fistular.

The Effect of Drug Abuse on Family Members

In addition to personal adversities, the abuse of alcohol and other drugs by youth may result in family crises, separation, devoice, and jeopardize many aspects of family life, sometimes resulting in family dysfunction. Both siblings and parents are profoundly affected by alcohol- and drug abuse family members would be regarded as an outcast t, irresponsible, abuse of drugs can drain a family's financial and emotional resources (Bureau of Justice Statistics, 1992).as money and other resources they have would spend unwisely, only to rehabilitate their child, they also leave in fear of murder from their addicted children, some even tend to kill their parents, There's a stigma attached to addiction in society, and there's a lot of guilt and shame for the individual's families who struggle with the condition. The family members become frustrated and sell all they have only to rehabilitate their children.

The Effect of Drug Abuse on the Community

The effect of drug abuse in the community is that most of the community members leave in fear of rubbery, thieves, peer group influence, by initiating others to take drugs, become gamblers, rapist, the incidence of murder and suicide, increase in crime cost on the community to build rehabilitation centres and to search for train personnel, rearing of unfruitful youths and the society will die out, the worst of it poverty cycle continues.

Figure 1V

Prevention of Abuse of Drugs

Parental monitoring and supervision are critical for drug abuse prevention. These skills can be enhanced with training on rule-setting; techniques for monitoring activities; praise for appropriate behaviour; and moderate, consistent discipline that enforces defined family rules.

- Avoid addiction to all these substances.
- Create awareness about the side effects and the consequences of the addiction. Of drugs
- Treatment of the people who are already addicted. With drugs
- Provide moral support and counselling for both addiction and none addicted.
- Avoid any kind of temptations and peer pressure.

Consider other strategies to prevent teen drug abuse:

Know your teen's activities. Pay attention to your teen's whereabouts. ...

Establish rules and consequences. For your teens ...

Parents should Know their teen's friends and the homes they come from..

Keep track of prescription drugs. ...

Parents should Provide support. ...

Parents should Set a good example.

VII. Conclusion

Youth now days see drugs. as a pleasure and fashion it is a most that every youth growing in this community should be part of it if not you will not be tolerated in some gatherings, taking of drugs as part of their food on a daily bases and these have made most of the youth both boys and girls dropping out of school becoming rapist, murderers, gabblers, thieves' rubbers and making themselves unfit in the community, *addiction cause a lot of disease and disability in the community as majority of them are moto bike (okada) ridders who after taking drugs will drive or ride home, they mostly involved in an accident which lead to death or disability* 'employment, and social economy have great effect on drug users.

VIII. Recommendation

1. The government to make rules, policies and regulations on proper used of certain drugs, eg painkiller drugs should be prescribe by a medical personnel.
2. Parents should monitor their children and the type of friends they have.
3. The used, dangers of drugs should be included in the curriculum at junior secondary school level as a compulsory module.
4. Government to take track of of possible areas drugs are sold and frequent checks.

5. Government to set up rehabilitation centres for those already addicted.
6. All other non-Governmental organizations dealing with youth and children to teach them about the dangers of drugs.

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On Research of Pharmacological Activity of "Bioil", Polyunsaturated Fatty Acids Concentrate

By Olena Koshova, Serhii Tanshyn, Nataliia Filimonova, Iryna Tishchenko, Nataliia Dubinina, Olena Shakun & Olga Geyderikh

National University of Pharmacy

Introduction- Polyunsaturated fatty acids (PUFAs) Are involved in the building of cell membranes of the brain, of the visual analyzer, and biological membranes of other organs and tissues. Due to this, they play an important 7 role in 5 the life of humans 8 and animals and are an essential factor of nutrition [1].

Fatty acids are the main component of all types of lipids. They vary in length of the carbon chain (short-chain, middle- chain, long-chain), in the presence of double bonds (saturated, monounsaturated, and 12 polyunsaturated fatty acids: di-, tri-, tetra-, penta- and hexa-). Based on the location of the first double bond at 3, 6, 7 or 9th carbon atom relatively the methyl end of the molecule, PUFAs are divided into families of ω-3, ω-6, ω-7, and 16 ω-9 respectively [2].

Keywords: *reparative, anti-inflammatory, polyunsaturated fatty acids, "bioil".*

GJMR-B Classification: *NLMC Code: WB 330*

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Olena Koshova [α], Serhii Tanshyn [σ], Nataliia Filimonova [ρ], Iryna Tishchenko [ω], Nataliia Dubinina [¥], Olena Shakun [§] & Olga Geyderikh [χ]

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I. Introducion

Polyunsaturated fatty acids (PUFAs) Are involved in the building of cell membranes of the brain, of the visual analyzer, and biological membranes of other organs and tissues. Due to this, they play an important 7 role in 5 the life of humans 8 and animals and are an essential factor of nutrition [1].

Fatty acids are the main component of all types of lipids. They vary in length of the carbon chain (short-chain, middle- chain, long-chain), in the presence of double bonds (saturated, monounsaturated, and 12 polyunsaturated fatty acids: di-, tri-, tetra-, penta- and hexa-). Based on the location of the first double bond at 3, 6, 7 or 9th carbon atom relatively the methyl end of the molecule, PUFAs are divided into families of ω-3, ω-6, ω-7, and 16 ω-9 respectively [2].

Synthesis of saturated FA occurs in liver cells, intestinal wall, lung, and adipose tissue, brain tissue, kidney, mammary gland during lactation through consistent extension of the carbon chain. Then, affected by enzyme- desaturases, monounsaturated FA is produced (for instance, oleic acid 18:1 of the ω-9 family). However, the human body can't synthesize linoleic (18:2 of the ω-6 family) and α-linolenic (18:3 of the ω-3 family) acids, which are essential for humans and must enter the organism with food [2].

The main representatives of PUFAs are linoleic, α- and γ-linolenic, arachidonic, eicosapentaenoic, docosahexaenoic acids. Linoleic and linolenic acids are predecessors of more long-chain fatty acids. Arachidonic acid is the substrate for the synthesis of eicosanoids, leukotrienes and prostaglandins, which are biological regulators of the cardiovascular, nervous, reproductive and immune systems.

Polyunsaturated fatty acids are widely used in medicine, pharmaceutical industry, cosmetics, nutrition etc. They are necessary for normal development of the human body and especially children. They are essential for preventing immune, inflammatory, cardiovascular diseases (rheumatoid arthritis, coronary heart disease, cancer).

The main sources of PUFAs of the ω-6 family are mainly various vegetable oils, PUFAs of the ω-3 family are found in large quantities in fish, seafood, egg yolk [3,4]. Linoleic and α-linolenic polyunsaturated fatty acids are essential acids, they are not synthesized de novo and must enter the body externally with food or as part of dietary products. Most dietary supplements contain PUFA in the form of triglycerides, which accumulate in adipose tissue, where, as needed by the body, they undergo lipolysis to form free fatty acids. The latter enter the bloodstream into cells where energy is required.

The most promising, in our opinion, is the use of PUFA in the form of organic acids, which have greater bioavailability, as they bypass the complex process of formation of triglycerides. Short- and medium-chain fatty acids (but not fatty acids with longer chains, which are too large to get directly through the small openings of the intestinal capillaries), entering the body are directly absorbed into the blood through the capillaries of the intestinal tract, pass through the portal vein, and others nutrients get into different organs.

In connection with the above, the staff of the limited liability company (LLC) "STAR TRADE COMPANY" has developed a technology for production of double distilled fatty acid concentratr "BIOIL" by bidistillation of various vegetable oils in the ratio ω-3: ω-3:: ω-9 acids - 1: 2.5: 3, respectively.

The purpose of this study was to study the reparative and anti-inflammatory properties of the

Author α: PhD, Senior Scientific Researcher, Associate Professor, Department of Microbiology, Virology and Immunology, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002.
e-mail: elenko926734@gmail.com
Author σ: Head of Limited Liability company "STAR TRADE COMPANY", Sicheslavska Naberezhna, budynok 29-A, misto Dnipro, Dnipropetrovska obl., 49000. e-mail: startradecompanyukr@3g.ua
Author ρ: Doctor of medical science, professor, head of department of microbiology, virology and microbiology, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002.
e-mail: natafilimanova@gmail.com
Author ω ¥: PhD, Associate Professor, Associate Professor, Department of Microbiology, Virology and Immunology, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002.
e-mails: irina2okt@gmail.com, dubininanata13@gmail.com
Author §: PhD, Senior Scientific Researcher, Associate Professor, Department of Microbiology, Virology and Immunology, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002.
e-mail: lekashakun@ukr.net
Author χ: Associate Professor, Associate Professor, Department of Microbiology, Virology and Immunology, National University of Pharmacy, Pushkinska str., 53, Kharkiv, Ukraine, 61002.
e-mail: ogejderih@gmail.com

concentrate of PUFA "BIOIL", produced by LLC "STAR TRADE COMPANY".

The study is standardized by regulatory documents and included in a set of pre-clinical studies required for the registration of medicines. The study was conducted by the guidelines and requirements of GLP and the Orders of MOH of Ukraine № 944 dated 14.12.2009 and № 95 dated16.02.2009 [5, 6].

II. Materials and Methods

Research of pharmacological activity of PUFAs concentrate "BIOIL" was performed on 3-4 months mature male inbred rats of 180-200 g. Before the experiment, animals had acclimatization for seven days in a room for testing. During the acclimatization everyday review of each animal was performed (assessing behavior and general physical condition). Healthy animals, which met the selection criteria, were distributed in experimental groups. Groups were formed by randomization (random selection) using body weight as the main criteria for distribution (deviation of initial weight between groups and within groups did not exceed ±10%).

The animals were kept in rooms with controlled microclimate parameters: air temperature +20-24 °C, humidity 45-65%, light regimen "12 hours day/night", in plastic cages of 6 animals. Airing of rooms and air sterilization were performed using quartz lamps daily. Animals had free access to water. Tap water was used for drinking. The animals consumed pelleted balanced feed (ТУ.У15.7-2123600159-001:2007). The animals were cared for according to standard operating procedures.

Estimation of reparative properties of PUFAs concentrate "BIOIL" was conducted on a model of full-surface stencil wounds in rats. Animals in research groups were anesthetized with sodium thiopental in the dose of 35 mg/kg. On the back area of 4×5cm was cleaned, outlined using marker stencil in order to receive wound of size 1,5×1,5 см. Then with a pair of scissors, cut the contour of full-surface wounds [1]. Treatment with TS was started within 2 hours after surgery, and it was continued once daily until complete healing of wounds.

The test sample was applied as a thin layer using a pipette in quantities of 1 ml/animal. Methyluracil ointment was chosen as a reference agent, pronounced reparative activity. The efficiency of the samples was assessed by planimetric indices: area of wounds and speed of wounds healing, which were determined on 3, 5, 8, 11, 14 days of the experiment.

Anti-inflammatory properties of PUFAs concentrate "BIOIL" was studied on a model of acute paw inflammation in rats weighing 180-200 g, caused by carrageenan. Acute edema in rats was caused by sub-plantar injection in right rear foot of carrageenan (0,1 ml/animal) [7, 8, 16].

According to Di Rosa et all, the dynamics of swelling caused by carrageenan [9], de-pends on the action of various transmitters: biogenic amines, kinins and prostaglandins, that are being released during the experiment. However, the leading role in the mechanism of acute inflammation in this model plays a release of prostaglandins as a result of activation of cyclooxygenase pathway of arachidonic acid oxidation [10, 11].

Gel diclofenac sodium 1% of JSC "Farmak", Kiev, Ukraine, was used as a reference agent (RA). Studied agents were applied on the damaged leg twice: once after injection of phlogogenic agent and after 1 hour. The development of edema was observed in dynamics: within 1, 2, 3, 4 and 5 hours (in terms of carrageenan edema). The volume of paws was measured using mechanical oncometer.

Antiexudative activity (AEA) of agents was determined by the degree of reduction of edema in experimental animals compared to control, and was calculated by the formula and is expressed in %:

$$AEA = \frac{\Delta Vc - \Delta Vt}{\Delta Vc} \times 100\%,$$

where:

AEA – antiexudative activity in %;

ΔVc – the average difference in volume between the legs with edema and without edema control group;

ΔVt – the average difference in volume between the legs with edema and without edema in test group.

The next step was to study the anti-inflammatory activity of PUFAs concentrate "BIOIL" on a model of proctitis in rats [12,13].

Experiments were performed on 24 white female inbred rats weighing 170-220 g. Suppositories "Relief" were chosen as a reference agent.

Experimental proctitis was simulated by two-times administration of 5% formalin solu-tion in dose of 0,2 ml/animal (at intervals of every other day) in rectum to a depth of 1.5 cm. Damaging agent administered in the morning fasting through metal probe after reflectory bowel evacuation [13]. The frequency of administration and concentration of formalin solution was selected so as to simulate inflammation and damage of rectal mucosa and to minimize general toxic effect of chemical substance.

Investigated agents were administered 24 hours after the first injection of formalin and 1 hour after the second administration of formalin, and later – once a day for the entire period of the experiment. The duration of treatment was ten days. PUFAs concentrate "BIOIL" was administered intragastric at a dose of 1 ml/kg and rectal (1 ml/kg).

Pharmacotherapeuic effect was evaluated by their effect on the clinical course of the disease comparing to intact and control groups. Efficacy criteria were: general condition of the animals, the presence and severity of clinical manifestations of disease (swelling of soft tissues around anus, purulent discharge from the anus). The dynamics of body weight and rectal temperature (using an electronic thermometer, model ТРЕМ-1) were estimated before proctitis was simulated on 7 and 10 days. Complete blood count was made on 7 and 10 day of treatment [14].

On day 10 of the experiment macroscopic changes of rectal mucosa were evaluated. The planimetric indices were determined: condition of rectal mucosa in points and area of affected part of rectal mucosa (mm^2). Semiquantitative evaluation of certain signs of inflammation was performed in points according to severity of edema, hyperemia, hemorrhage availability:

0 points - no signes;
1 point - a sign expressed slightly;
2 points - a sign expressed moderately;
3 points - a sign expressed pronounced.

Degree of damage was assessed by summing the scores for these parameters.

For statistical conclusions when comparing samples of variables was used one-way anal-ysis of variance (or Kruskal-Wallis test for variables that are not subject to the normal law of distribution), which revealed differences between the experimental groups, and after Newman-Keuls test or Mann-Whitney test. Differences between groups were considered statistically significant at $p < 0,05$ [15,16,17]. Standard statistical software package Statistica 6.0 and Excel were used for the mathematical and statistical calculations.

III. Results of the Study

Research of the reparative activity of PUFAs concentrate "BIOIL"

It was established that in rats, which received applications of PUFAs concentrate "BIO-IL", one day after simulation of full-surface stencil wounds there was observed an improvement of condition of wound surface: wound edges and wound itself were clean and tidy, the area of the wound was smaller than in animals that were not treated (Figure 1).

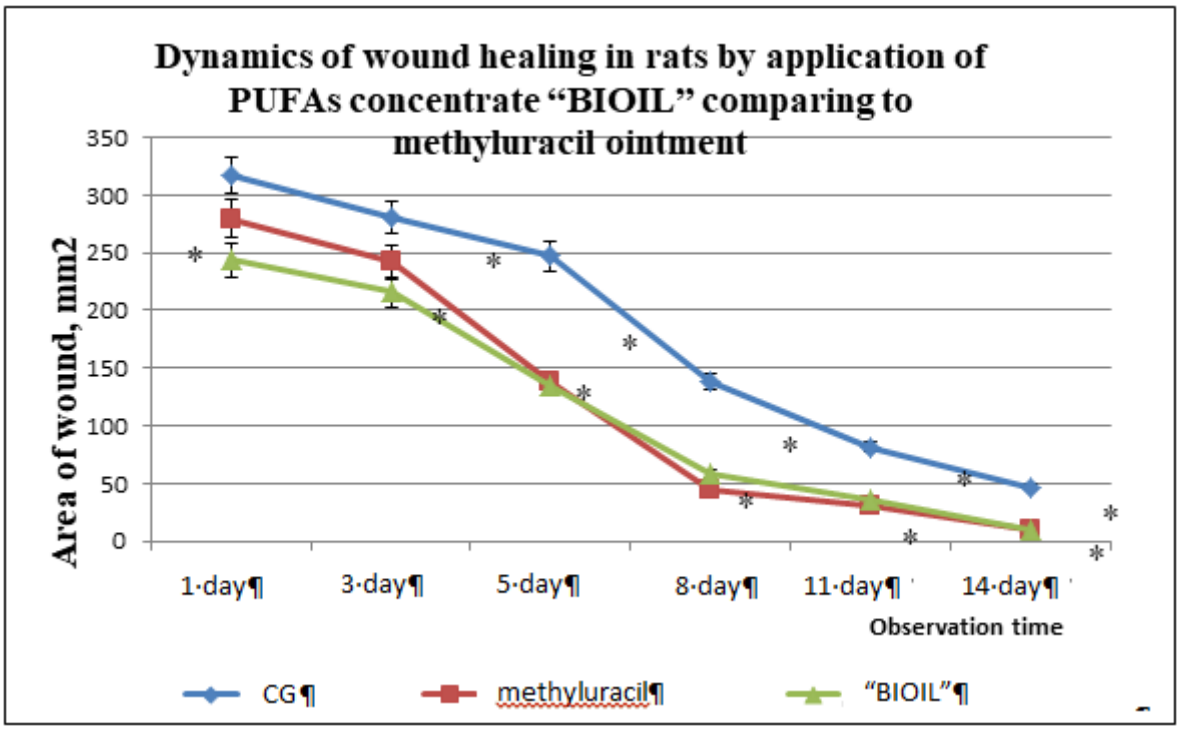

Figure 1: Reparative activity of PUFAs concentrate "BIOIL" on a model of full-surface stencil wounds in rats, n=6

Notes:

1. *– statistically significant differences comparing to control group, $p<0,05$;
2. ** – statistically significant differences comparing to reference agent, $p<0,05$;
3. CG– control group;
4. Methyluracil –reference agent (RA);
5. "BIOIL" – PUFAs concentrate "BIOIL".

Later on reparative activity of the TS increased. According to the received data, the highest reparative activity PUFAs concentrate "BIOIL" showed at 5-8 day of observation, an evidence of this was a significant reduction in wound area in rats by 1,8 and 2,3 times comparing to rats that were no treated (figure 1). Rate of wound healing in this group increased 2 and 1.5 times correspondingly (figure 2). In terms of long-term follow-up (11-14 days), the rate of healing under influence of TS slightly decreased, but was significantly higher than in rats from the control group. It should be emphasized that PUFAs concentrate "BIOIL" was not inferior to that reference agent methyluracil ointment, which has a pronounced reparative effect (figure 1, 2). In the initial stage of PUFAs concentrate "BIOIL" application its reparative activity was even more effective than methyluracil ointment.

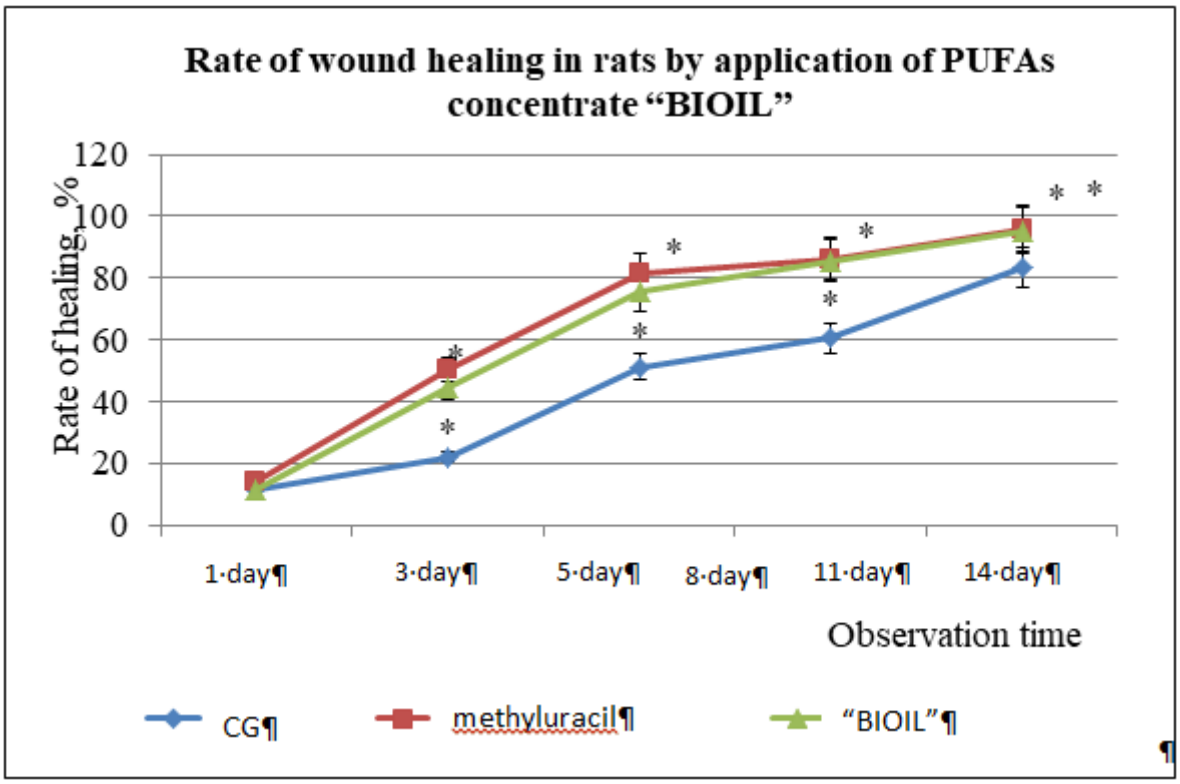

Figure 2: Effect of PUFA concentrate "BIOIL" on rate of wound healing in rats with simulated full-surface stencil wounds, n=6

Notes:

1. *– statistically significant differences comparing to control group, $p<0,05$;
2. ** – statistically significant differences comparing to reference agent, $p<0,05$;
3. CG– control group;
4. Methyluracil –reference agent (RA);
5. "BIOIL" – PUFAs concentrate "BIOIL".

Thus, established expressive reparative activity of PUFAs concentrate "BIOIL" on a model of full-surface stencil wounds is achieved by presence in test-sample of omega-6 class, in particular linoleic, which is the basic component of the intercellular lipids and is contained in structural elements of membranes' phospholipids. Long-chain ceramides are up to 40 % of the lipid matrix. They contain linoleic acid [18]. Gamma-linolenic acid, which is formed from linoleic acid under the influence of the enzyme delta six desaturase, controls the homeostasis of the skin by supporting the barrier function, fluidity and permeability of membranes, preventing transepidermal water loss. It was established that even at minor violations of transdermal barrier keratinocytes induce release of cytokines that regulate the process of restoring the horny layer of the skin. If there is excessive damage to the horny layer of the skin, an inflammatory reaction starts [19]. Application of PUFAs concentrate "BIOIL" on the wound surface protects layers of the skin, that surround the wound surface, and prevents transepidermal water loss. In addition, another essential PUFA – arachidonic acid is formed from γ-linolenic acid. This acid is a substrate for the synthesis of eicosanoids (prostaglandins, leukotrienes), that regulate the inflammatory and immunological processes. Hence, at PUFAs "BIOIL" complex entry in the dermis, it starts the repair

processes that contributes to faster wound healing in rats.

Research of antiexudative activity of PUFAs concentrate "BIOIL" at skin application on a model of paw inflammation caused by carrageenan

Results of the study listed in Table 1 showed that reference agent (RA) gel "Ortofen", 1% had stable antiexudative activity starting from one hour of the experiment (Table 1). The average anti-inflammatory activity (AIA) of reference agent was 55% (табл. 1).

PUFAs concentrate "BIOIL" has a uniform anti-inflammatory activity by reducing the severity of edema in an average of 20% (Table 2). It is known that PUFAs of ω-3 and ω-6 class are precursors to eicosanoids forming – biologically active substances of lipid nature (prostag-landins, leukotrienes, thromboxane, etc.), that regulate local cellular and tissue functions, including inflammatory reactions, functioning of platelets, leukocytes and erythrocytes, constriction and vasodilatation etc. [20,21]. Carrageenan activates the metabolism of arachidonic acid and prostaglandin synthesis, which causes the development of inflammation of the paw of rats. When applied to the leg by penetration through the skin barrier α-linolenic acid, which is part of PUFAs concentrate "BIOIL", replaces arachidonic acid in phospholipids of cell membranes and contributes to the synthesis of eicosanoids of an anti-inflammatory action. It is known that the functional properties of eicosanoids, synthesized from arachidonic acid and ω3 fatty acid (α-linolenic acid), have opposite effects. For example, prostacyclin 3, formed from ω3 fatty acids, has a vasodilatory effect and decrease arterial pressure. Prostacyclin 2, which is synthesized from arachidonic acid, on the contrary, is a vasoconstrictive agent. These differences are also found in leukotrienes synthesis (LS). Leukotrienes of Series 5 (LT5), synthesized from ω3 fatty acids, have an anti-inflammatory effect, while Leukotrienes of Series 4 (LT4), synthesized from ω6 fatty acids (arachidonic acid), are an inductor of inflammatory reactions cascade. But intensity of anti-inflammatory action of eicosanoids, formed from ω3 fatty acids, is less pronounced, which causes a mild anti-inflammatory effect [22,23]. This explains the stable anti-inflammatory action of PUFAs concentrate "BIOIL" in experiment.

Thus, on the model of paw inflammation caused by carrageenan in rats it was established that PUFAs concentrate "BIOIL" has a stable anti-inflammatory activity, which on average was up to 20%.

Table 1: Influence of PUFAs concentrate "BIOIL" on dynamics of paw edema in rats induced by carrageenan, n=6, *M (Min÷Max)*

Animal groups	Indices	Observation time					
		1 hour	2 hours	3 hours	4 hours	5 hours	Average AIA, %
Control group	ΔV, cu	12,50 (11÷17)	14,50 (11÷18)	17,83 (12÷22)	20,17 (15÷24)	16,17 (11÷25)	-
Gel diclofenac sodium, 1%	ΔV, cu	7,67(3÷10)*	8,33(5÷11)*	8,33 (4÷14)*	8,33 (2÷14)*	8,00(5÷12)*	55
	AA,%	69	43	51	59	51	
PUFAs concentrate "BIOIL"	ΔV, cu	10,17 (6÷13)	11,83(8÷17) **	14,33 (8÷23) t**	15,17 (8÷24) */**	13,67 (9÷20) **	20
	AIA, %	19	18	20	25	16	

Notes:

1. *– differences statistically significant comparing to control group, p<0,05;
2. ** – differences statistically significant comparing to control group, p<0,05;
3. t – tendency to statistical significance, 0,05<p<0,100;
4. ΔV – difference between the swollen paws and its original size, cu
5. AIA – anti-inflammatory activity.

Determination of anti-inflammatory action of PUFAs concentrate "BIOIL" on a model of proctitis in rats

The course of destructive and inflammatory diseases of the rectum (hemorrhoids, procti-tis, paraproctitis, proctosigmoiditis) is a relevant problem in modern medicine, due to the severity of these diseases and their prevalence [13]. Because of uncertainty in etiology and absence of a unified pathogenesis theory, pharmacotherapy for this group of diseases is complex and often inefficient, which determine the rationale for

finding and developing new drugs to treat diseases of the rectum.

Natural compounds are interesting as objects for research – unsaturated fatty acids, which have low toxicity and have a wide range of pharmacological activity [1, 14].

Taking into account pathogenetic mechanisms of proctitis, valuable are antioxidant, anti-inflammatory, membrane-stabilizing, antibacterial and reparative properties of polyunsaturated fatty acids [1, 6]. The literature data and research results show pronounced reparative properties of PUFAs in various pathologies.

Expressive anti-inflammatory properties of PUFAs concentrate "BIOIL" were established in the previous experiment and justify assumption of its effectiveness in experimental proctitis.

According to the data presented in Tables 2-5, experimental proctitis was characterized by severe clinical signs of the disease. In animals of the control group diarrhea, swelling of the soft tissues around the anus, purulent discharge from the anus, weight loss (Table 2), increased rectal temperature (Table 3) were observed, which indicated a severity of inflammation and reduction of trophic processes due to a general toxication of animals.

Table 2: Influence of PUFAs concentrate "BIOIL" on gain of body weight in terms of experimental proctitis, *Me (25Q;75Q)*

Animal groups	Gain of body weight, g
Intact group	10,8 (0; 20)
Control group	-9 (-45; 35)*
PUFAs concentrate "BIOIL"	10 (10;30)**
Suppositories "Relief"	14 (0; 25)

Notes:
1. *– differences statistically significant comparing to intact group, $p<0,05$;
2. **– differences statistically significant comparing to control group, $p<0,05$.

Table 3: Influence of PUFAs concentrate "BIOIL" on dynamics of body temperature in rats in terms of experimental proctitis, *Me (25Q;75Q)*

Animal groups	Temperature, ^{0}c		
	Baseline data	7 day	10 day
Intact group	37, 2 (36,7; 37,5)	37,1 (36,7; 37,8)	37,1 (36,7; 37,7)
Control group	37,3 (37,1; 37,6)	38,9 (38,0; 39,7)*	38,0 (37,8; 38,2)*
PUFAs concentrate "BIOIL"	37,2 (36,7; 37,5)	38,3 (37,7; 39,1)*	37,4 (36,9; 37,7)**
Suppositories "Relief"	37,1 (36,6; 37,5)	38,6 (35,4; 39,6)*	36,8 (36,3; 38,0)**

Notes:
1. *– differences statistically significant comparing to intact group, $p<0,05$;
2. **–differences statistically significant comparing to control group, $p<0,05$.

The severity of the pathology was confirmed by pronounced leukocytosis: on the 7th day the number of leukocytes statistically significant increased by 2,3 times, and on 10th day – by 1,7 times. This is an evidence of the development of systemic inflammation (Table 4).

Treatment with test agents significantly weakened the course of experimental pathology. The combined administration of PUFAs concentrate "BIOIL" in terms of proctitis in rats, contributed to the improvement of tissues trophic and general condition of the animals. Reduction in severity of clinical signs of disease, statistically significant increase in body weight and decrease of body temperature to a level of intact animals was an evidence of this (Tables 2-3).

When using PUFAs concentrate "BIOIL" there was a reduce of number of white blood cells and hemoglobin count recovery, indicating anti-inflammatory properties of the investigational product (Table 4).

Table 4: Influence of PUFAs concentrate "BIOIL" on dynamics of hematological parameters in rats under the experimental proctitis, *Mean±St.er.*

Indices	Observation time	Animal groups			
		Intact group	Control group	PUFAs concentrate "BIOIL"	Suppositories "Relief"
Red blood cells, 10^{12}L	7 day	5,12±0,13	4,82±0,14	5,03±0,06	4,89±0,04
	10 day	5,15±0,06	5,08±0,06±	5,08±0,7	5,23±0,08

Hemoglobin, g/L	7 day	131,8±7,93	121,7±8,5	127,1±4,8	120,0±4,4
	10 day	132,6±4,21	116,2±7,24	131,3±5,50	150,2±9,23**
White blood cells, 10^{12}L	7 day	18,75±1,03	42,38±5,97*	34,35±3,95*	32,92±5,00*
	10 day	20,88±4,03	35,15±2,41*	28,25±1,25	23,15±2,98**

Notes:

1. *– differences statistically significant comparing to intact group, $p<0,05$;
2. **– differences statistically significant comparing to control group, $p<0,05$.

By the use of suppositories "Relief" a similar dynamics of investigated parameters was observed (Tables 2-4).

Results of clinical observations are consistent with the macroscopic data. Significant damage of colon was revealed at autopsy in animals from control group at autopsy: lesion area was equal to 415,80 mm^2, the severity of inflammation was assessed at 6,4 points (Table 5, figure 3).

While using PUFAs concentrate "BIOIL" colon mucosa quickly came back to normal, no signs of necrosis, hemorrhage or congestion were detected at any animal from the group (Table 5, figure 3).

Suppositories "Relief" did the same expressive effect as test-sample: mucosa colon was in normal condition without congestion and edema (Table 5, figure 3).

Table 5: Influence of PUFAs concentrate "BIOIL" on planimetric indices of colon dam-age severity in rats in terms of experimental proctitis, *Mean±St.er.*

Animal groups	Planimetric indices	
	Affected area, mm^2	Total point
Control group	415,80±80,27	6,40±0,68
PUFAs concentrate "BIOIL"	0,0±0,0*	0,0±0,0*
Suppositories "Relief"	0,0±0,0*	0,0±0,0*

Notes:

1. *– differences statistically significant comparing to Control group, $p<0,05$;
2. **– differences statistically significant comparing to control group, $p<0,05$.

Therefore, the experimental model of proctitis in rats showed pronounced efficacy of PUFAs concentrate "BIOIL". PUFAs concentrate "BIOIL" was not inferior than reference agent suppositories "Relief" within influence on trophic processes, severity of inflammation. It proves that test agent has distinctive anti-inflammatory, reparative and general metabolic properties.

Analyzing received data and based on literature data, we can assume that efficacy of PUFAs concentrate "BIOIL" on a model of experimental proctitis was caused by reduction of production of proinflammatory eicosanoids (prostaglandin E2, leukotriene B4) from arachidonic acid, increase of production of anti-inflammatory eicosanoids (prostaglandin E3, leukotriene B5), reduction (due to inhibition of leukotriene B4 synthesis) of synthesis of platelet aggregation factor, interleukin-1 and tumor necrosis factor - cytokines that play a leading role in diseases of the rectum and various inflammatory diseases. Received results provide the background for promising usage of PUFAs concentrate "BIOIL" in the treatment and prevention of various inflammatory diseases with autoimmune and/or allergic component such as rheumatoid arthritis, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, asthma, atopic dermatitis, inflammatory diseases of the line colon and others.

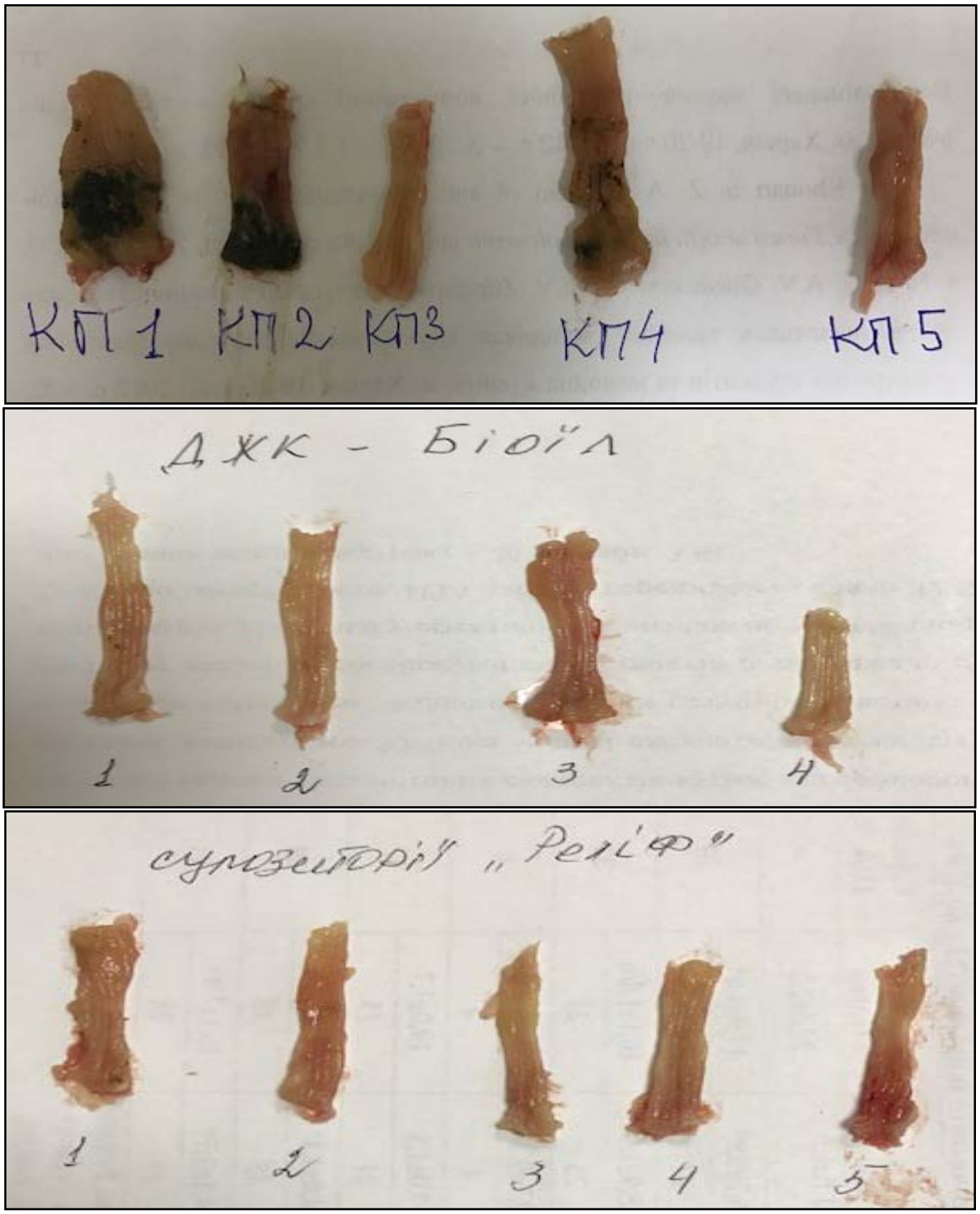

Figure 3: Influence of PUFAs concentrate "BIOIL" on macroscopic characteristics of experimental proctitis.

A – colon of animals from the control group. Large areas of necrosis, hemorrhage and edema of the mucosa.
B – colon of animals that received PUFAs concentrate "BIOIL" in combined mode (intragastric and rectal). Necrosis and hemorrhage are absent, normal mucosa.
C – colon of animals that received suppositories "Relief". Mucosa of the colon without any visible signs of damage.

IV. Conclusions

1. Reparative action of PUFAs concentrate "BIOIL" was determined on a model of full-surface stencil wounds in rats. According to expressiveness of efficiency PUFAs concentrate "BIOIL" is not inferior to Methyluracil ointment.

2. On the model of acute inflammation PUFAs concentrate "BIOIL" had moderate anti-inflammatory effect, reducing paw edema in experimental rats.
3. On a model of experimental proctitis in rats, it was determined an expressive efficacy of PUFAs concentrate "BIOIL". PUFAs concentrate "BIOIL" was not inferior than suppositories "Relief". According to influence on trophic processes, intensity of inflammation in colon mucosa of animals from PUFAs concentrate "BIOIL" was not inferior than suppositories "Relief". This is an evidence of its profound anti-inflammatory, reparative and general metabolic action.

List of Symbols, Characters, Units, Abbreviations and Terms

GLP – Good Laboratory Practice
m – error of the sample mean
M – mean of sample
ДЕЦ МОЗ – State Expert Center of the MoH of Ukraine
IG – intact group
CG – control group
PUFAs – Polyunsaturated fatty acids
RS – reference-sample
TS – test-sample
RA – reference agent
AIA – anti-inflammatory activity

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Relationship between Oxidative Stress and Diabetes Mellitus

By Dharmender & Abdul Hafeez

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Keywords: mellitus diabetes (DM), type 2 diabetes mellitus (T2DM), 1 DM (T1DM), reactive oxygen species (ROS), superoxide dismutase (SOD), catalase (CAT), and glutathione (GLT), malondialdehyde (MDA); insulin receptor substrates (IRSs).

GJMR-B Classification: NLMC Code: WK 810

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Dharmender [α] & Abdul Hafeez [σ]

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I. Introduction

DM is a metabolic disorder characterized by high levels of free glucose in the blood. Diabetes is a disorder in the human body that causes blood glucose (sugar) levels to rise above normal due to insulin secretion or insulin resistance. This is also called hyperglycaemia (1). DM is an incurable disease that has a detrimental effect on many metabolic pathways and contributes to the pathophysiology of diabetic complications (2, 3). Oxidative stress is a very important factor in the development of diabetes (8). Oxidative stress is known to be associated with lifestyle-related diseases including atherosclerosis, high blood pressure, and diabetes. Free radical forms are important for body parts in biological homeostasis (11, 12), but where their production is excessive and greater than the body's antioxidant capacity, then the effects of oxidative stress (12). Oxidative stress is a major factor in the development of diabetes and insulin resistance (12-14), triggering pathophysiologic pathways and initiating a burst of malignant pathways leading to insulin resistance and DM (8, 15). In this review, we discussed the potential roles of oxidative stress in building insulin resistance and DM.

Author α: Glocal School of Pharmacy, Glocal University, Mirzapur Pole, Saharanpur, Uttar Pradesh, India.
Corresponding Author σ: Associate Professor, Department of Pharmaceutics, Glocal School of Pharmacy, Glocal University, 247121. e-mail: Hafeezpharmacist007@gmail.com

II. Classification of Diabetes Mellitus

There are different types of DM, but the most common subtypes are 1 DM (T1DM) and 2 DM type (T2DM). T1DM occurs due to beta-cell dysfunction, reduced insulin secretion, and low levels of circulating insulin. T2DM is the most common type of DM that accounts for approximately 90–95% of patients with diabetes and is mainly associated with insufficient response to insulin (reduced insulin sensitivity) and insulin resistance in borderline tissues (16). With type 2 diabetes, the human body does not use insulin properly. This is called insulin resistance. Initially, pancreas produces extra insulin to make it. Over time the pancreas may not be able to cope and it may not produce enough insulin to maintain normal blood sugar levels. Type 2 can be controlled by improving lifestyle, oral hypoglycaemic therapy, and insulin. Pregnancy diabetes is another topic that occurs in women during pregnancy when the body is less sensitive to insulin. Pregnancy diabetes does not occur in all women and usually develops after childbirth (17). Other types of DM are adolescent diabetes which is diabetes mellitus, pre-existing diabetes in adults, and secondary diabetes from other diseases such as pancreatitis or secondary to the use of drugs such as corticosteroids (18, 19).

III. Oxidative Stress and Antioxidant Process

Various normal cells produce free radicals such as aerobic respiratory products and other metabolic processes (7) including reactive oxygen species (ROS). ROS is a highly active oxidant and can have adverse effects on cellular lipids, proteins, and DNA or reactive oxygen species (ROS) produced by organisms due to normal cell metabolism and environmental factors, such as air pollution or cigarette smoke. ROS are highly active molecules and can damage cell formation such as carbohydrates, nucleic acids, lipids, and proteins and alter their functions. Cells usually contain enzymes and coenzymes that act as antioxidants. This helps to reduce ROS and prevents it from causing damage (6). Oxidative stress is defined as an imbalance between the chemical processes responsible for the production of active oxygen (ROS) and those responsible for the removal of ROS (20). There are many enzymes in the cell that have internal mechanisms such as superoxide dismutase (SOD), catalase (CAT), and glutathione

(GLT), which protect cells from free radicals (25). Some heavy metal products have free properties such as iron (ferric) and copper (26) that can mix proteins, lipids, and nucleic acids and produce toxic products that lead to tissue dysfunction (27,28). They alter the structure of biologic molecules and break them down (28). DNA fragmentation is a well-known result of oxidative stress, which affects genetic expression and cell survival (23). Malondialdehyde (MDA), total cholesterol, and active hydroperoxides (ROOH) are oxidative stress biomarkers that occur in diabetic patients. (30). Oxidative stress plays important roles in diabetic complications through lipid peroxidation, DNA damage, and mitochondrial dysfunction (13, 23, 31, 32). Its involvement has been shown in other illnesses and age-related problems such as cardiovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, neurological diseases, and cancer and more. Including high free varieties (33). Many scientists believe that the theory of oxidative evolution is a major cause of aging and related problems (33). Problems caused by oxidative stress and insulin resistance are prevented with the help of redox biology (34).

IV. Normal Insulin Signaling Pathways and Insulin Resistance

Insulin is usually a 51 amino acid dipeptide containing a series A and B series linked to 2 disulfide bonds found in cysteine residues. The chain contains 21 amino acids and the B chain contains 30 amino acids. Insulin is encoded by a short arm of chromosome 11 in pancreatic β-cells containing signal peptide, chain B, connective peptide (and A) and A chain (4,5). In proinsulin, C-peptide binding is enclosed at each end by the dibasic residues (Arg-Arg and Lys-Arg) that link the N-terminus of the A series and the C-terminus of the B chain (124,125). Proinsulin made from Golgi substances is converted to insulin by removing dibasic residues by trypsin-like endyprotease enzymes such as insulin and C-peptide (5). Insulin resistance is a key factor in T2DM where cells are unable to respond to insulin effectively (8, 35) There are different enzymes and mediators, which facilitate the entry of glucose into adipocytes, muscles, and myocardial cells via GLUT- 4 (glucose transporter- 4) transporters [8, 34]. The feature is triggered by binding insulin to α chain of insulin receptors (IRs), which are members of transmembrane tyrosine kinases that are made up of α and-chains and activated by insulin and IGF- (insulin-like growth -) 1 and IGF-2 (36). As a result, binding induces structural changes in the chain by autophosphorylation in tyrosine residues through different adapter proteins, namely, insulin receptor substrates (IRSs), Shc proteins (SHC-transforming), and APS protein (protein adapter) (37,38)). These processes provide a suitable site for binding IRS-1 (insulin receptor substrate-1) (38). Many types of insulin-dependent kinases such as extracellular protein kinase C, S6K1 (ribosomal protein S6 kinase beta-1), serine / - threonine-protein kinase 2, protein kinase B etc and other types of kinases such as AMP-activated protein kinase and glycogen synthase kinase 3 can activate and activate phosphorylate IRS (38, 39). The activated IRS-1 binds to PI3K (phosphoinositide 3-kinase) and activates it, which, in turn, promotes the conversion of PIP2 (phosphatidylinositol 4,5-bisphosphate) to PIP3 (phosphatidylinositol 3,4,5-trisphosphate) (40). PIP3 itself is a potent activator of Akt, which also contributes to cell-induced glucose uptake through the production of GLUT-4 and inhibits glycogen synthase kinase leading to increased glycogen secretion (40, 41). Any disruption in the above-mentioned steps may cause insulin resistance and DM (34).

V. Relationship between Oxidative Stress and Insulin Resistance

Oxidative stress increases the risk of insulin resistance and DM (26, 34). It should be noted that oxidative stress caused by DM has more complex interactions (42, 43). The following are potential molecular mechanisms by which free radicals disrupt the normal glucose Homeostasis contributes to the formation of DM.

a) β-Cell Dysfunction/Insulin Production and Secretion

The function of insulin is to maintain blood glucose levels by promoting glucose uptake into insulin-targeted tissues. Glucose is a key regulator of insulin secretion by pancreatic Beta cells, which triggers a burst of events called beta-stimulating cells - the ability to sense circulating blood sugar levels and release the right amount of insulin to keep blood glucose at a normal level (126- 129).

Normal glucose homeostasis is made up of healthy and active beta cells and DM is associated with various levels of beta-cell dysfunction (44, 45). DM occurs as a result of loss of beta-cell function and function (46). In these cases, insulin secretion produced by glucose from beta cells is reduced and decreased; therefore, glucose levels have risen above normal levels (47). In this process, insulin secretion occurs, which is interrupted by a decrease in the energy of the sugar to promote insulin secretion leading to severe unstable insulin release and followed by beta-cell failure (46). Beta-cell dysfunction occurs due to pathogenic mechanisms and oxidative stress (46, 48). Free radicals in pancreatic beta cells arise due to enzyme activity such as mitochondrial respiratory tract (MRC) and NADPH (nicotinamide adenine dinucleotide phosphate) oxidase or NOX enzyme (15, 49-51). Superoxide anion is a major free radical pathway produced by MRC and NOX enzyme in beta cells (52). Beta cells are affected by free radicals produced by phagocytic and immune

cells (53). Chronic hyperglycemia induces free radical production in the islands by increasing cytosolic calcium and protein kinase activation pathways (50, 54). Beta cells have a low dose of antioxidant protection system, so that oxidative stress on beta cells increases in DM and plays an important role in the loss of their function in both T1DM and T2DM (45, 48, 55). Oxidative stress disrupts beta-cell function through a number of molecular mechanisms (48, 55-62). Significantly reduces insulin production, disrupts the insertion of proinsulin vesicles into plasma membranes, and reduces their exocytosis in response to glucose distribution (48, 55, 56). It can also cause apoptotic processes in pancreatic cells that lead to death and loss of beta cells (48, 55, 56,). Therefore, depressive beta cell dysfunction caused by stress is a major potential target for experimental intervention in patients with DM. We suggest that pharmacologic agents protecting the islands from oxidative damage may provide Target therapeutics to promote beta-cell function that leads to improved glucose homeostasis.

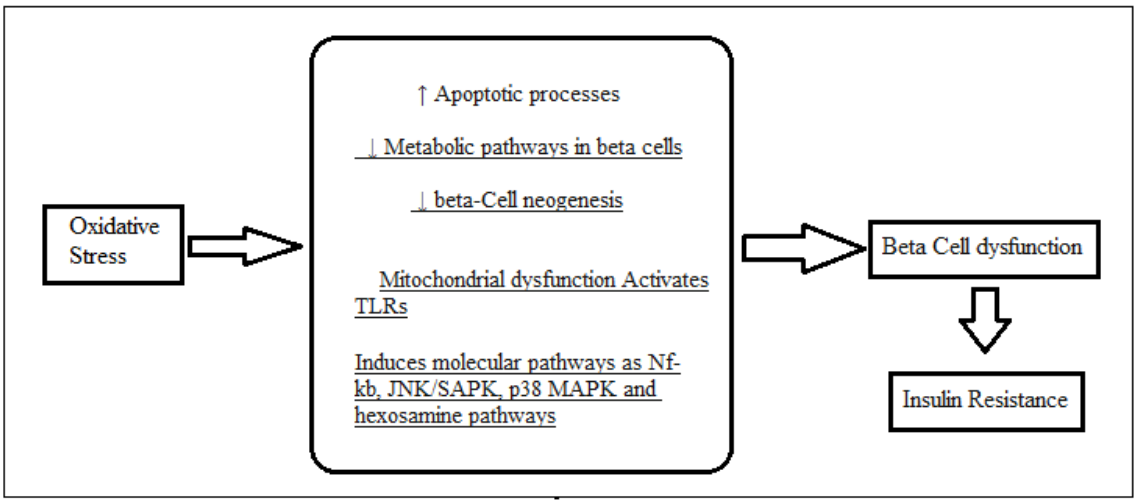

Figure 1: Possible molecular mechanisms between oxidative stress and beta-cell dysfunction

b) GLUT-4 Expression and/or Localization

GLUT4 is an insulin-regulated glucose Transporter found in adipose tissue and bound muscles such as skeletal and heart muscle and, therefore, to maintain insulin sensitivity in these tissues a normal body profile of GLUT-4 expression and / or localization is required (15,63). The reducing factor of the GLUT-4 antagonist has an effect on insulin sensitivity (63, 64) as a decrease in glucose entering target cells translates into lower insulin sensitivity in these tissues (65). According to Clinical Studies GLUT-4 expression and / or localization decreased insulin-resistant and T2DM-resistant patients (64, 66, 67). This patho physiologic condition is exacerbated by oxidative stress (68, 69). Oxidative stress can reduce the content of GLUT-4 by impairing gene expression by damaging the binding of the nuclear material to the GLUT-4-induced insulin receptor in 3T3-L1 adipocytes (70). 3T3-L1 adipocytes develop oxidative stress in these cells and receive Glut-4 expression from these tissues. They found that hydrogen peroxide produced by significant oxidative stress is regulated by GLUT-4 to 3T3-L1 adipocytes and, consequently, reduces cellular glucose (70). Other studies suggest that oxidative stress reduced GLUT-4 transport to cell membranes. They induced mitochondrial oxidative stress using mitochondria-targeted paraquat to adipocytes and found that oxidative stress significantly reduced GLUT-4 transport and thus induced insulin resistance in these tissues (71). Long-term oxidative stress can suppress transcription factors involved in GLUT-4 expression such as peroxisome proliferator-activated receptor gamma, CCAAT-binding proteins, factor 1, MEF2 (myocyte enhancer factor 2), and Nf- κb etc. (70, 72-74). It can also suppress small amounts of RNA involved in GLUT-4 expression such as miR-21a-5p, miR-222- 3p, miR-29c-3p, and miR-133a-3p etc (75-78). In addition, a variety of stress-inducing substances and products such as p38 MAPK, JNK / SAPK, PKC (protein kinase C), sorbitol, and hexosamine are all produced by oxidative damage and may suppress GLUT-4 (29). Therefore, reduced expression / activation of GLUT-4 is one of the major molecular mechanisms by which oxidative stress induces insulin resistance and contributes to the formation of DM (15).

c) Insulin Signaling Pathways

Insulin resistance with DM occurred due to any impairment in insulin signaling pathways (79, 80). In appreciation of insulin sensitivity was introduced novel therapeutic variables of the insulin signal (80). Oxidative stress can disrupt normal IST (insulin signal transduction) at various levels including IR, IRS-1 and IRS-2; PI3K enzyme and Akt signature methods (81-86). T2DM-induced oxidative stress and IST substances in

the brains of diabetic mice caused by Balbaa and colleagues in 2017 (87). They found that oxidative stress significantly reduced the expression of an IST substance such as p-IRS, p-AKT, and GSK-3β in brain tissue with normal insulin signaling (87). Oxidative stress induced IRS-1 and IRS-2 serine phosphorylation, leading to disrupted IST (81, 82). Free radicals can induce serine phosphorylation of IRS-1 and suppress normal IST using JNK / SAPK signaling methods (85). Other types of serine / threonine kinases such as Akt (or PKB), GSK-3, AMPK, and mTOR are also very sensitive to oxidative stress and may interfere with insulin signaling (100-102). Oxidative stress can also lead to IST impairment by down-regulating proteins involved in normal IST (87). IST substances such as Akt, IRS, IRS-1, and GSK-3 are under the influence of low free radicals regulated by oxidative stress thus interfering with insulin sensitivity leading to insulin resistance and DM (87). Therefore, IST disruption is another important link between oxidative stress and insulin resistance (81-86, 88-90).

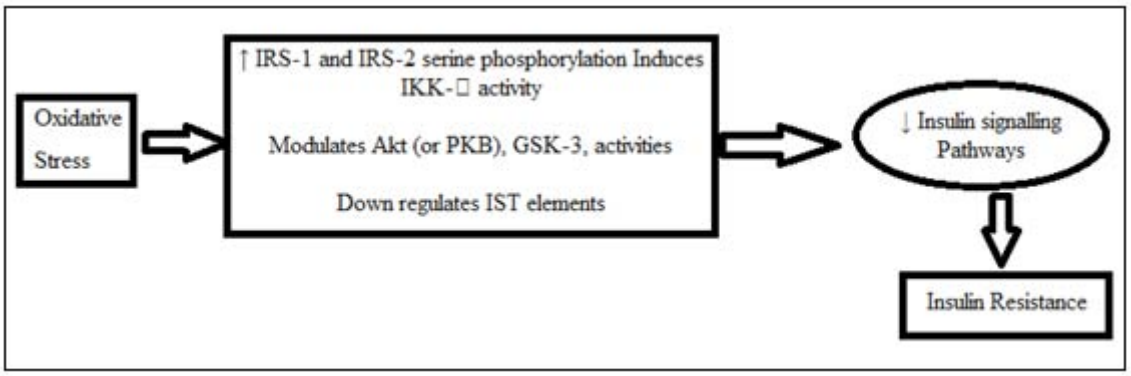

Figure 2: Oxidative stress impairs insulin signaling pathways by several molecular pathways.

d) Inflammatory Processes

The inflammatory response is one of the main molecular mechanisms involved in the pathophysiology of insulin resistance, DM, and related complications (53, 91, 92). A separate study suggests that chronic inflammation is involved in the pathophysiology of insulin resistance DM (92-98). This type of mechanism can also establish other pathophysiologic mechanisms of DM such as beta-cell dysfunction (53, 95). Animal experimental and pathological studies show that IR and inflammation are directly linked during T2DM development (24,42) Inflammatory mediators play an important role in improving IR and T2DM by activating various inflammatory responses such as IL -β. IL- a is an effective pro-inflammatory mediator that plays an important role in controlling various inflammatory mediators such as cytokines, adipokines and chemicals. It causes inflammation by binding to interleukin-1 receptor type I (IL-1RI) and reduces the expression of insulin receptor substrate-1 (IRS-1) at the ERK-dependent writing level and the post-transcriptional ERK level (43)). IL-1β production is largely controlled by dietary stress caused by diet. Other experimental studies have been performed on a variety of experimental animals to investigate the presence of various inflammatory responses in β-cells that indicate that IL-β plays a key role in activating other inflammatory mediators such as cytokines and chemicals (21, 22). in cell-cells of pancreatic islands due to impaired insulin secretion occurs in β-cells of pancreatic islands. In this way IL-β also plays an important role in causing inflammation of the tissues of the body because it reduces the ability of the insulin receptors to respond to glucose which ultimately leads to the formation of IR in borderline tissues. IL-6 is another mediator that can be positively linked to IR [19 - 22]. IL-6 not only inhibits the metabolism of non-oxidative glucose (120,121) but also suppresses the activity of lipoprotein lipase which increases plasma levels of triglycerides [23]. In addition, IL-6 also activates cytokine signaling proteins (SOCS) (101,108) that can inhibit cytokine transcriptional factor activation of the insulin receptor [26] causing IR development in borderline tissue.

TNF-α is another mediator in which TNF-α improved interactions between IR and T2DM (122,123) Experimental studies show that TNF-α expression increases in obese animals that modulate insulin action (135). From previous studies it has been found that serum levels of TNF-α are positively correlated with IR pathophysiology (135, 136) indicating that TNF-α is also a key factor contributing to IR development. There are many monocytes, macrophage activity and mediators such as CX3CL1 (fractalkine), CRP 4 Oxidative Medicine and Cellular Longevity, IL-18, MCP-1 (monocyte chemo attractant protein-1), resistin, PAI-1 (plasminogen activator inhibitor -1), E-selectin, and IFN-γ (interferon-gamma)-induced IR (91, 94-98).

Therefore, by making inflammatory processes a therapeutic approach for the management of diabetes (93,103,104). Several studies have reported the importance of anti-inflammatory agents in glucose homeostasis. For example, Goldfine and colleagues in 2010 examined the effects of sugar reduction salsalate (salicylate prodrug) and reported that it was effective in

reducing HbA1c and fasting plasma glucose in T2DM patients (105). Clinical trials have been performed with agents to reduce oxidative stress. Oxidative stress is a major inflammatory event as it stimulates the formation of monocytes and macrophages that promote inflammatory responses involved in insulin resistance and DM (103,106,107). It also regulates the expression of pro cytokines and thus enhances inflammatory mediators (88, 108). Thus, free radical-induced inflammation is one of the possible links between oxidative stress and insulin resistance (99).

e) Mitochondrial Dysfunction

Mitochondria are cellular organelles that play a key role in energy production, reactive oxygen species (ROS), mediator signaling (130-133), apoptosis (9,10) calcium storage, heat production, and cell survival and act as part of the signal signal pathways (109,110). Mitochondria are major sources of ROS (134) production that cause mitochondrial dysfunction, insulin resistance and DM (111). Oxidative stress is an important factor contributing to mitochondrial dysfunction (112), which impairs mitochondrial function by altering normal MRC activity, reducing mitochondrial respiratory capacity, increasing proton leakage to MRC, which alters potential fluid differentiation internal mitochondrial., and reduced the integrity of the mitochondrial layers (113-115). These processes can occur in pancreatic islands and / or systematically in adipocytes and muscle tissue (116). The normal process of glucose uptake depends largely on the body's function of healthy mitochondria that produce the energy needed to receive glucose from borderline tissues (117). Thus, mitochondrial dysfunction significantly reduces ATP cell production and interferes with cellular glucose uptake (88). As a result of these cells they fail to take up circulating glucose in response to insulin leading to insulin resistance (88, 16,118). In addition, oxidative stress can disrupt normal mitochondrial function by increasing the production of mitochondrial fatty acid oxidation and DAG (diacyl glycerol), which also stimulates many serine / threonine kinases leading to IST impairment (88). Thus, stress-dependent mitochondrial dysfunction is another molecular mechanism by which free radicals induce insulin resistance (88, 116,118). Oxidative stress and mitochondrial dysfunction have two interactions where both can produce energy (119).

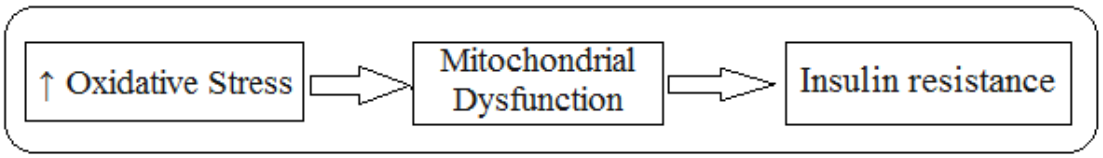

Figure 3: Oxidative stress induces insulin resistance.

VI. Conclusion

Diabetes is a metabolic disorder due to hyperglycaemia that can be completely cured but not normally controlled. There are many factors that contribute to the increase and progression of diabetes. Factors can be genetics, stress, obesity, and unhealthy lifestyle etc. But above all oxidative stress plays an important role in the development and progression of diabetes. Oxidation is a chemical process within the human body that leads to the production of free radicals. These oxidative reactions produce free radicals that slowly damage cells and organs by removing inflammatory mediators (such as TNF-α, cytokines, adipokines and chemicals etc.) and causing damage to cell organelles such as mitochondrial damage, damage of ribosomal, nucleus damage etc. leading to insulin resistance. Among other things, oxidative stress increases the rate of disease progression by interfering with insulin signaling pathways resulting in a decrease in insulin sensitivity. Oxidative stress increases apoptosis necrosis leading to beta cell dysfunction leading to insulin secretion. Antioxidants play a very important role in eliminating free radicals. They bind with free oxidative radicals and remove them from the body by making it harder. Combining antioxidant treatment with standard hypoglycaemic medications will increase recovery rate and antioxidant therapy will help address diabetes problems such as nephrotoxicity, neuropathy and retinopathy, which may be caused by oxidative stress.

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Isolation and Study of Dry Extract from Echinacea Purpurea

By Z.A. Zuparova & G.M. Ismoilova

Abstract- Medicines based on echinacea can be attributed to the group of herbal remedies that increase the activity of nonspecific factors of the body's defence and the immune system. The stimulation of bone marrow haematopoiesis with echinacea preparations increases the number of leukocytes and spleen RES cells. Echinacea preparations have a mild, multivalent effect and practically no side effects. A dry extract was obtained from the herb Echinacea purpurea by polyextraction.

The conditions for extraction and the extractants were selected, and the kinetics of extraction, isolation and purification of the extract from the herb Echinacea purpurea were studied.

Keywords: echinacea purpurea, dry extract, extractants, extraction kinetics, flavonoids, hydroxycinnamic acids, polysaccharides, monosaccharides.

GJMR-B Classification: NLMC Code: QV 55

Strictly as per the compliance and regulations of:

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Z.A. Zuparova [α] & G.M. Ismoilova [σ]

Abstract- Medicines based on echinacea can be attributed to the group of herbal remedies that increase the activity of nonspecific factors of the body's defence and the immune system. The stimulation of bone marrow haematopoiesis with echinacea preparations increases the number of leukocytes and spleen RES cells. Echinacea preparations have a mild, multivalent effect and practically no side effects. A dry extract was obtained from the herb Echinacea purpurea by polyextraction.

The conditions for extraction and the extractants were selected, and the kinetics of extraction, isolation and purification of the extract from the herb Echinacea purpurea were studied.

Based on the studies carried out, the extract was found to contain flavonoids, hydroxycinnamic acids, tannins, amino acids, and polysaccharides.

The polysaccharide hydrolysate contained monosaccharides such as uronic acids, galactose, trace amounts of glucose, arabinose, xylose, and sucrose from ketosaccharides. The main monosaccharides making up the polysaccharide were uronic acids and arabinose.

Keywords: echinacea purpurea, dry extract, extractants, extraction kinetics, flavonoids, hydroxycinnamic acids, polysaccharides, monosaccharides.

I. Introduction

Currently, there is a wide range of secondary immunodeficiencies associated with urbanization, chemization, and increased stress load, leading to disruptions in the functioning of the immune system. Such conditions require immunocorrection. Substances that stimulate the body's nonspecific defence must be effective, available, and harmless. In this regard, a special place is occupied by research related to the introduction of herbal medicines into medical practice, the study of their chemical composition, and the optimization of technologies for obtaining such medicines. Herbal remedies have been used in medicine as long as the concept of treating diseases has existed. For thousands of years, mankind has used herbal medicines for therapeutic purposes. Vegetable raw materials are environmentally friendly, and their use is based on the close relationship of the human body and natural components. The search for new types of raw materials and the study of previously used plants as potential sources for obtaining drugs with immunomodulatory action is relevant [1,2]. Medicines based on echinacea belong to the group of herbal remedies that increase the activity of nonspecific factors of the body's defence and the immune system. The stimulation of bone marrow haematopoiesis with echinacea preparations increases the number of leukocytes and spleen RES cells. Echinacea preparations have a mild, multivalent effect and practically no side effects [3,4].

Echinacea preparations are used in medical practice as immunomodulatory agents. The biologically active substances they contain activate the protective cells of the immune system - phagocytes. Preparations of this plant, in addition to immunomodulatory properties, are used in the treatment of tumours. Juice from fresh inflorescences effectively promotes blood clotting and wound healing.

In folk medicine, echinacea is used for colds, flu, blood poisoning, diseases of the bladder, urticaria, burns, herpes, heavy metal poisoning, liver diseases and diabetes. Echinacea-based preparations have a depressing effect on streptococci, Escherichia coli and the influenza virus.

II. Materials and Methods

To obtain a dry extract by polyextraction, dried Echinacea purpurea was used as a starting material. Qualitative assessment of flavonoids was carried out by TLC and chemical-analytical reactions. TLC was carried out on "Mesk" chromatographic plates with 60 F 254silica gel on an aluminium substrate (10X15 cm) in the solvent system n-butanol - acetic acid - water (4: 2: 1), with standard samples of rutin, luteolin, and quercetin for comparison. Zones of adsorption were detected under UV light at a wavelength of 254 nm. After chromatography, the chromatographic plate was dried in a drying oven at a temperature of 100-105 °C (Table 1).

Additionally, for the qualitative detection of flavonoids, reactions with caustic soda were carried out. The qualitative detection of oxycinnamic acids was carried out by the paper chromatography method in a chromatographic chamber with 2% acetic acid as a mobile phase. Tannins were detected with ammonium iron alum. Qualitative detection of amino acids was carried out using the ninhydrin reaction. Qualitative

Author α: Ph.D,. teaching assistant, Department of Organization of Pharmaceutical Production and Quality Management, Tashkent Pharmaceutical institute, Tashkent, Uzbekistan.
e-mail: author.uzb@mail.ru
Author σ: Ph.D, Associate Professor, Department of Organization of Pharmaceutical Production and Quality Management, Tashkent Pharmaceutical Institute, Tashkent, Uzbekistan.

detection of alkaloids was carried out using silicotungstic acid.

III. Results

Selection of extractant. The extraction process of the dark red echinacea surface was studied to select a moderate extractant. Purified water and 40%, 70%, and 96% ethyl alcohol were used as extractants. Then, 0.5 kg of raw material was placed in an extractor with a volume of 5 l, and the extractant was poured in until a glassy surface was formed. The extraction was carried out at room temperature. Every 8 hours, the extract in the extractor was poured out, and fresh solvent was poured in until a glassy surface was formed on the surface of the raw material. This process was repeated 4 times. The extracts from each extractor were combined and determined based on the content of chlorogenic acid, polysaccharides and extractives (see Figure 1).

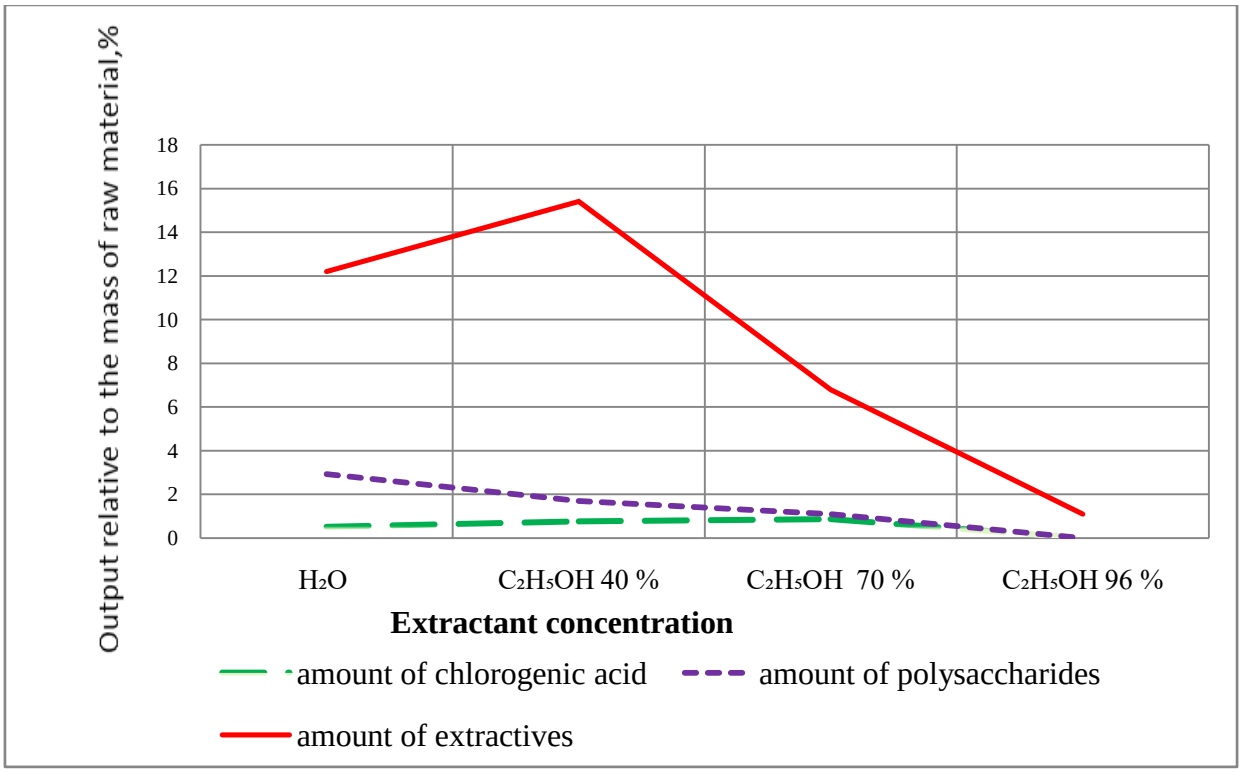

Figure 1: Influence of extractant type on the release of biologically active substances

The curves in the figure show that the amount of chlorogenic acid is highest in the extract obtained in 70% ethyl alcohol, the amount of polysaccharides was highest in the aqueous separation, and the amount of extractives was highest in the separation in 40% ethyl alcohol. For this reason, the polyextraction method was selected as a moderate method to obtain a dry extract with an immunomodulatory effect from the dark red echinacea plant.

Selection of raw material fineness level. The raw material of dark red echinacea was crushed and passed through sieves of different diameters. Then, 0.5 kg of raw materials of different fineness levels was taken from each batch and placed in 5 extractors with a capacity of 5 l. Raw materials smaller than 2 mm were placed in the first extractor, 2-5 mm in the second extractor, 5-8 mm in the third extractor, 8-11 in the fourth extractor, and more than 14 mm in the fifth extractor. Extraction was performed 3 times, first with 70% ethyl alcohol, then with 40% ethyl alcohol, and finally with water. Every 8 hours, the separation was removed and combined. The combined extracts were tested for the amount of flavonoids and extractives (see Figure 2).

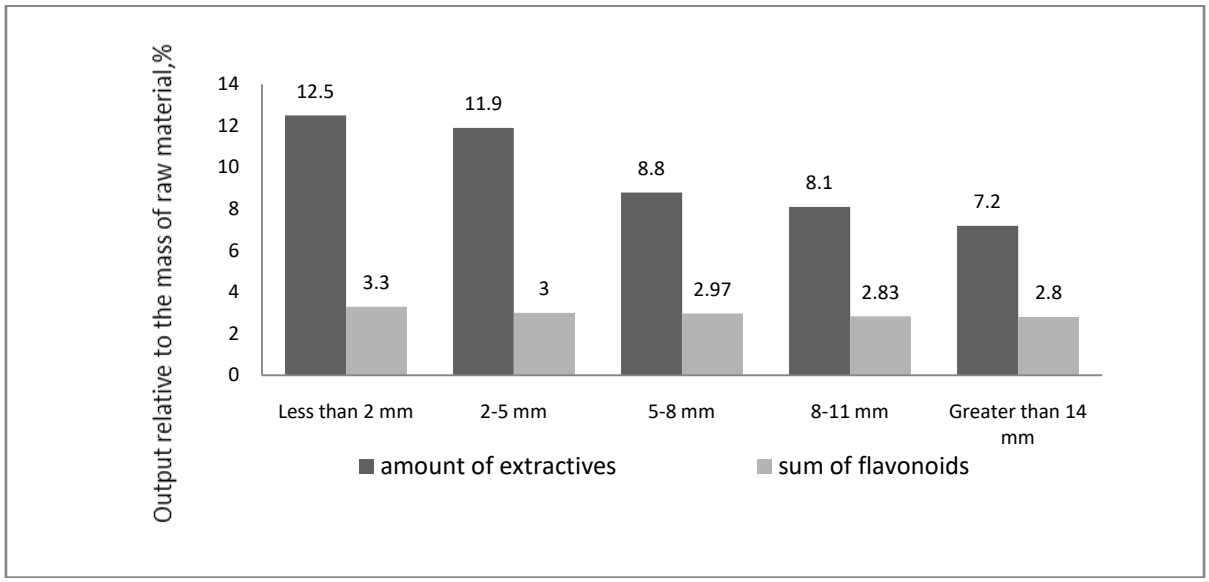

Figure 2: The effect of the degree of fineness of the raw material on the release of flavonoid aggregates

The rate of separation of flavonoids from the 2 mm raw material was high, but the resulting extract was turbid and difficult to filter. The extraction rate from the raw material was slow. The yield of flavonoids from crushed raw materials of 5-8 mm and 8-11 mm was lower than that of crushed raw material of 2-5 mm. *To isolate flavonoids, a dark red echinacea raw material of 2–5 mm in size was selected as suitable.*

Temperature selection. The temperature factor plays an important role in the separation of biologically active substances. As the temperature increases, the extraction rate also increases due to the increase in the diffusion rate.

To select the most appropriate temperature, 2-5 mm crushed raw material was placed in 4 extractors with a volume of 0.5 kg to 5 l and treated with 70% ethyl alcohol until a glassy surface was formed. Extraction in the first extractor was carried out at room temperature of 20-30 °C, in the second extractor at 30-40 °C, in the third extractor at 40-50 °C and in the fourth extractor at 50-60 °C. Extraction was not carried out at temperatures above 60 °C, as the efficiency of separation of biologically active substances was almost unchanged (see Figure 3).

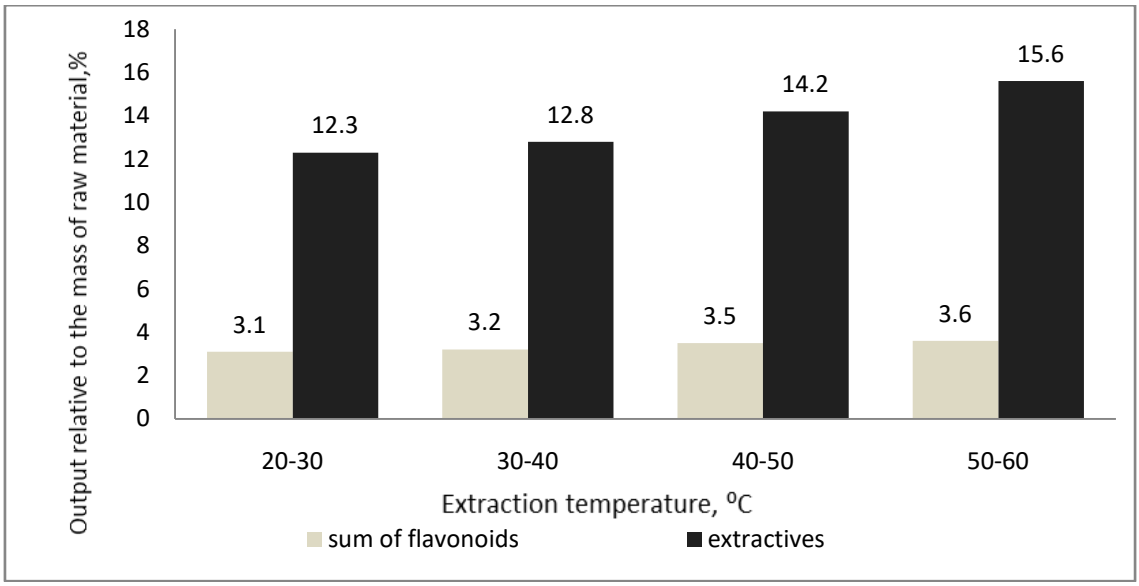

Figure 3: The effect of temperature on the level of flavonoid release

According to the data in the picture, the release of extractives at the temperature of 50-60 °C was the highest, but the total flavonoids was almost from the same as that obtained at 20-40 °C. Accordingly, the separation of flavonoid aggregates from dark red echinacea raw material at room temperature was found to be appropriate.

Purification of the extract. Extraction in a liquid–liquid system is the most widely used extract purification method. Therefore, to purify the concentrated alcoholic extract of dark red echinacea, nonaqueous organic solvents such as hexane, acetone, chloroform, and extraction gasoline were used. The experiment was carried out as follows: 0.5 kg of crushed raw material with a size of 2-5 mm was placed in an extractor with a volume of 5 l. It was first extracted with 70% ethyl alcohol, then with 40% ethyl alcohol, and then with purified water for 5 hours. The resulting extracts were combined and divided into 4 equal parts. Each part of the extract was concentrated at a temperature of 60-700 °C and a vacuum of -0.6...- 0.4 kgf/cm^3 to 1.2 l. Water was added in a 1:1 ratio. The first aqueous solution was treated 3 times with 0.5 l of hexane, the second with acetone, the third with chloroform, and the fourth with extraction gasoline. The separations in each reactor were analysed. The results of the analysis revealed a high degree of clarity of the extract treated with chloroform and a low content of lipophilic substances and chlorophyll.

Obtaining dry extract of dark red echinacea by polyextraction.

Five kilograms of 2-5 mm air-dried, weighed dark red echinacea was placed in a KD-2KY extractor and covered with 70% ethyl alcohol until a glassy surface was formed. The extractor was hermetically sealed and extracted by suffocation for 6 hours. Extraction was carried out at room temperature. After the allotted time, 15 l of the first separation was poured off. The extraction was repeated by adding 40% ethyl alcohol to the extractor until a glassy layer was formed on the surface of the raw material. After 6 h, 15 l of the separation was poured off. For the third extraction, purified water was poured over the raw material. Extraction took 6 hours. *The third separation was 15 l. The first, second, and third separations were combined and transferred to the collector through a multilayer fabric filter.* The filtered separation was evaporated from 20-25 l in a rotor vacuum evaporator at 70-80 °C and -0.8-0.4 kgf/cm^2. A total of 11.2 l of concentrated alcohol extract was poured from the vacuum evaporator into the reactor and diluted with 10 l of water. The resulting aqueous extract was treated 3 times with 1.0 chloroform. The purified separation in chloroform was evaporated in a rotary vacuum evaporator at 50-60 °C and -0.6-0.8 kgf/cm^2. The purified extract was then dried in a spray dryer.

IV. Discussion

A greenish brown powder with a characteristic odour was isolated. A phytochemical study of the isolated dry extract from the herb *Echinacea purpurea* was carried out to create an effective drug or standardized extract with pharmacological effects, including immunomodulatory effects.

The data obtained are shown in the Table 1.

Table 1: The qualitative composition of some biologically active substances in the dry extract of Echinacea purpurea

Substances	Analysis methods and conditions	Analytical effect of reaction
1	2	3
Flavonoids	Reaction: with caustic soda	Yellow staining
Hydroxycinnamic acids	Paper chromatography method, mobile phase 2% acetic acid solution	Blue fluorescence of spots underUV light
Tannins	Reaction with ammonium iron alum	Dark green colouration
Amino acids	Reaction with 0.1% ninhydrin	Red and purple spots

The studies carried out on the extract revealed the presence of flavonoids, hydroxycinnamic acids, tannins, and amino acids [5,6].

The immunomodulatory effect of *Echinacea purpurea* preparations is due to the sum of biologically active substances, but the main immunomodulatory effect is due to polysaccharides [7,8,9].

The following fractions were isolated:

- Fraction of polysaccharides extracted with water at room temperature (VRPS-X) (ratio 1:20, precipitant 95% ethyl alcohol 1:3);
- Fraction of polysaccharides extracted with hot water (VRPS-G) (temperature 80 °C, ratio 1:20, precipitant 95% ethyl alcohol 1:3);
- Fraction of pectin substances (PV) (equal volumes of 0.5% solutions of oxalic acid and ammonium oxalate, ratio 1:20, temperature 70 °C, precipitant ethyl alcohol 1:5);
- fraction of hemicelluloses (HC) (0.5% potassium hydroxide, temperature 20 °C, ratio 1:20, precipitant ethyl alcohol 1:4).

The isolated fractions were subjected to acid hydrolysis (water-soluble polysaccharides were hydrolysed with 1 N H_2SO_4 for eight hours at 100 °C, pectin substances and hemicellulose-2n H_2SO_4 for 20 hours at 100 °C), neutralized with barium carbonate, demineralized using the KU-2 cation exchanger in H+ form. Then, monosaccharides were identified by paper chromatography and comparison with standard samples. Paper chromatography was performed on Filtrak-FN 18 paper in a butanol-1-pyridine-water (6: 4: 3) solvent system (system 1). Aniline phthalate acid

(developer 1) and a 5% urea solution (developer 2) were used to identify spots. Chromatograms were developed at 105-110 °C.

Water-soluble polysaccharides - the monosaccharide composition of the polysaccharide represented by uronic acids and neutral monosaccharides (system 1, developer 1).

Pectin substances- monosaccharide composition represented mainly by uronic acids, galactose, and arabinose (system 1, developer 1).

Hemicellulose structural components includinguronic acids and neutral monosaccharides (system 1, developer 1), mainly galactose; arabinose and xylose are less pronounced in paper chromatography.

The polysaccharide hydrolysate contained monosaccharides such as uronic acids, galactose, trace amounts of glucose, arabinose, and xylose. The main monosaccharides were uronic acids and arabinose.

When determining water-soluble polysaccharides, 0.5 ml of purified water was added to 20 ml of liquid extract, and hydrolysis of the polysaccharide was carried out for 12 hours at 1000 °C with 1 N sulfuric acid. The hydrolysate was neutralized with $BaCO_3$, filtered off and deionized with a KU-2 (H+) cation exchanger, evaporated and chromatographed in a butanol-pyridine-water solvent system at a ratio of 6:4:3 for 18 hours. The chromatogram was dried and treated with acidic aniline phthalate, revealing the presence of the following monosaccharides: uronic acids, galactose, trace amounts of glucose, arabinose, xylose, and from ketosaccharides, sucrose. The main monosaccharides were uronic acids and arabinose.

V. Conclusion

The conditions for extraction and the extractants were selected, and the kinetics of the extraction, isolation and purification of the extract from the herb Echinacea purpurea were studied.

Based on the studies carried out, the extract was found to contain flavonoids, hydroxycinnamic acids, tannins, amino acids, and polysaccharides.

The polysaccharide hydrolysate was found to containmonosaccharides such as uronic acids, galactose, trace amounts of glucose, arabinose, and xylose, as well assucrose from ketosaccharides. The main monosaccharides that make up the polysaccharides are uronic acids and arabinose.

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Appealing Decisions

Unless specified in the notification, the Editorial Board's decision on publication of the paper is final and cannot be appealed before making the major change in the manuscript.

Acknowledgments

Contributors to the research other than authors credited should be mentioned in Acknowledgments. The source of funding for the research can be included. Suppliers of resources may be mentioned along with their addresses.

Declaration of funding sources

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Preparing your Manuscript

Authors can submit papers and articles in an acceptable file format: MS Word (doc, docx), LaTeX (.tex, .zip or .rar including all of your files), Adobe PDF (.pdf), rich text format (.rtf), simple text document (.txt), Open Document Text (.odt), and Apple Pages (.pages). Our professional layout editors will format the entire paper according to our official guidelines. This is one of the highlights of publishing with Global Journals—authors should not be concerned about the formatting of their paper. Global Journals accepts articles and manuscripts in every major language, be it Spanish, Chinese, Japanese, Portuguese, Russian, French, German, Dutch, Italian, Greek, or any other national language, but the title, subtitle, and abstract should be in English. This will facilitate indexing and the pre-peer review process.

The following is the official style and template developed for publication of a research paper. Authors are not required to follow this style during the submission of the paper. It is just for reference purposes.

Manuscript Style Instruction (Optional)

- Microsoft Word Document Setting Instructions.
- Font type of all text should be Swis721 Lt BT.
- Page size: 8.27" x 11'", left margin: 0.65, right margin: 0.65, bottom margin: 0.75.
- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
- Abstract: font size 9 with the word "Abstract" in bold italics.
- Main text: font size 10 with two justified columns.
- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
- The paragraph before spacing of 1 pt and after of 0 pt.
- Line spacing of 1 pt.
- Large images must be in one column.
- The names of first main headings (Heading 1) must be in Roman font, capital letters, and font size of 10.
- The names of second main headings (Heading 2) must not include numbers and must be in italics with a font size of 10.

Structure and Format of Manuscript

The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

A research paper must include:

a) A title which should be relevant to the theme of the paper.
b) A summary, known as an abstract (less than 150 words), containing the major results and conclusions.
c) Up to 10 keywords that precisely identify the paper's subject, purpose, and focus.
d) An introduction, giving fundamental background objectives.
e) Resources and techniques with sufficient complete experimental details (wherever possible by reference) to permit repetition, sources of information must be given, and numerical methods must be specified by reference.
f) Results which should be presented concisely by well-designed tables and figures.
g) Suitable statistical data should also be given.
h) All data must have been gathered with attention to numerical detail in the planning stage.

Design has been recognized to be essential to experiments for a considerable time, and the editor has decided that any paper that appears not to have adequate numerical treatments of the data will be returned unrefereed.

i) Discussion should cover implications and consequences and not just recapitulate the results; conclusions should also be summarized.
j) There should be brief acknowledgments.
k) There ought to be references in the conventional format. Global Journals recommends APA format.

Authors should carefully consider the preparation of papers to ensure that they communicate effectively. Papers are much more likely to be accepted if they are carefully designed and laid out, contain few or no errors, are summarizing, and follow instructions. They will also be published with much fewer delays than those that require much technical and editorial correction.

The Editorial Board reserves the right to make literary corrections and suggestions to improve brevity.

Format Structure

It is necessary that authors take care in submitting a manuscript that is written in simple language and adheres to published guidelines.

All manuscripts submitted to Global Journals should include:

Title

The title page must carry an informative title that reflects the content, a running title (less than 45 characters together with spaces), names of the authors and co-authors, and the place(s) where the work was carried out.

Author details

The full postal address of any related author(s) must be specified.

Abstract

The abstract is the foundation of the research paper. It should be clear and concise and must contain the objective of the paper and inferences drawn. It is advised to not include big mathematical equations or complicated jargon.

Many researchers searching for information online will use search engines such as Google, Yahoo or others. By optimizing your paper for search engines, you will amplify the chance of someone finding it. In turn, this will make it more likely to be viewed and cited in further works. Global Journals has compiled these guidelines to facilitate you to maximize the web-friendliness of the most public part of your paper.

Keywords

A major lynchpin of research work for the writing of research papers is the keyword search, which one will employ to find both library and internet resources. Up to eleven keywords or very brief phrases have to be given to help data retrieval, mining, and indexing.

One must be persistent and creative in using keywords. An effective keyword search requires a strategy: planning of a list of possible keywords and phrases to try.

Choice of the main keywords is the first tool of writing a research paper. Research paper writing is an art. Keyword search should be as strategic as possible.

One should start brainstorming lists of potential keywords before even beginning searching. Think about the most important concepts related to research work. Ask, “What words would a source have to include to be truly valuable in a research paper?” Then consider synonyms for the important words.

It may take the discovery of only one important paper to steer in the right keyword direction because, in most databases, the keywords under which a research paper is abstracted are listed with the paper.

Numerical Methods

Numerical methods used should be transparent and, where appropriate, supported by references.

Abbreviations

Authors must list all the abbreviations used in the paper at the end of the paper or in a separate table before using them.

Formulas and equations

Authors are advised to submit any mathematical equation using either MathJax, KaTeX, or LaTeX, or in a very high-quality image.

Tables, Figures, and Figure Legends

Tables: Tables should be cautiously designed, uncrowned, and include only essential data. Each must have an Arabic number, e.g., Table 4, a self-explanatory caption, and be on a separate sheet. Authors must submit tables in an editable format and not as images. References to these tables (if any) must be mentioned accurately.

Figures

Figures are supposed to be submitted as separate files. Always include a citation in the text for each figure using Arabic numbers, e.g., Fig. 4. Artwork must be submitted online in vector electronic form or by emailing it.

Preparation of Eletronic Figures for Publication

Although low-quality images are sufficient for review purposes, print publication requires high-quality images to prevent the final product being blurred or fuzzy. Submit (possibly by e-mail) EPS (line art) or TIFF (halftone/ photographs) files only. MS PowerPoint and Word Graphics are unsuitable for printed pictures. Avoid using pixel-oriented software. Scans (TIFF only) should have a resolution of at least 350 dpi (halftone) or 700 to 1100 dpi (line drawings). Please give the data for figures in black and white or submit a Color Work Agreement form. EPS files must be saved with fonts embedded (and with a TIFF preview, if possible).

For scanned images, the scanning resolution at final image size ought to be as follows to ensure good reproduction: line art: >650 dpi; halftones (including gel photographs): >350 dpi; figures containing both halftone and line images: >650 dpi.

Color charges: Authors are advised to pay the full cost for the reproduction of their color artwork. Hence, please note that if there is color artwork in your manuscript when it is accepted for publication, we would require you to complete and return a Color Work Agreement form before your paper can be published. Also, you can email your editor to remove the color fee after acceptance of the paper.

Tips for writing a good quality Medical Research Paper

1. Choosing the topic: In most cases, the topic is selected by the interests of the author, but it can also be suggested by the guides. You can have several topics, and then judge which you are most comfortable with. This may be done by asking several questions of yourself, like "Will I be able to carry out a search in this area? Will I find all necessary resources to accomplish the search? Will I be able to find all information in this field area?" If the answer to this type of question is "yes," then you ought to choose that topic. In most cases, you may have to conduct surveys and visit several places. Also, you might have to do a lot of work to find all the rises and falls of the various data on that subject. Sometimes, detailed information plays a vital role, instead of short information. Evaluators are human: The first thing to remember is that evaluators are also human beings. They are not only meant for rejecting a paper. They are here to evaluate your paper. So present your best aspect.

2. Think like evaluators: If you are in confusion or getting demotivated because your paper may not be accepted by the evaluators, then think, and try to evaluate your paper like an evaluator. Try to understand what an evaluator wants in your research paper, and you will automatically have your answer. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

3. Ask your guides: If you are having any difficulty with your research, then do not hesitate to share your difficulty with your guide (if you have one). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work, then ask your supervisor to help you with an alternative. He or she might also provide you with a list of essential readings.

4. Use of computer is recommended: As you are doing research in the field of medical research then this point is quite obvious. Use right software: Always use good quality software packages. If you are not capable of judging good software, then you can lose the quality of your paper unknowingly. There are various programs available to help you which you can get through the internet.

5. Use the internet for help: An excellent start for your paper is using Google. It is a wondrous search engine, where you can have your doubts resolved. You may also read some answers for the frequent question of how to write your research paper or find a model research paper. You can download books from the internet. If you have all the required books, place importance on reading, selecting, and analyzing the specified information. Then sketch out your research paper. Use big pictures: You may use encyclopedias like Wikipedia to get pictures with the best resolution. At Global Journals, you should strictly follow here.

6. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right? It is a good habit which helps to not lose your continuity. You should always use bookmarks while searching on the internet also, which will make your search easier.

7. Revise what you wrote: When you write anything, always read it, summarize it, and then finalize it.

8. Make every effort: Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

9. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several unnecessary diagrams will degrade the quality of your paper by creating a hodgepodge. So always try to include diagrams which were made by you to improve the readability of your paper. Use of direct quotes: When you do research relevant to literature, history, or current affairs, then use of quotes becomes essential, but if the study is relevant to science, use of quotes is not preferable.

10. Use proper verb tense: Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

11. Pick a good study spot: Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

12. Know what you know: Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

13. Use good grammar: Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

14. Arrangement of information: Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

15. Never start at the last minute: Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

16. Multitasking in research is not good: Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

17. Never copy others' work: Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

18. Go to seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

19. Refresh your mind after intervals: Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.

20. Think technically: Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

21. Adding unnecessary information: Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

22. Report concluded results: Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

23. Upon conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

The introduction: This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear: Adhere to recommended page limits.

Mistakes to avoid:

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

Title page:

Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

Abstract: This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

Reason for writing the article—theory, overall issue, purpose.

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

Approach:

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

Introduction:

The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.

The following approach can create a valuable beginning:

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

Approach:

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

Procedures (methods and materials):

This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

When a technique is used that has been well-described in another section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show all particular resources and broad procedures so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step-by-step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

Materials may be reported in part of a section or else they may be recognized along with your measures.

Methods:

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

Approach:

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

What to keep away from:

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

Content:

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

What to stay away from:

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

Approach:

As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

Figures and tables:

If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

Discussion:

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an argument should be.

Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."

Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

The Administration Rules

Administration Rules to Be Strictly Followed before Submitting Your Research Paper to Global Journals Inc.

Please read the following rules and regulations carefully before submitting your research paper to Global Journals Inc. to avoid rejection.

Segment draft and final research paper: You have to strictly follow the template of a research paper, failing which your paper may get rejected. You are expected to write each part of the paper wholly on your own. The peer reviewers need to identify your own perspective of the concepts in your own terms. Please do not extract straight from any other source, and do not rephrase someone else's analysis. Do not allow anyone else to proofread your manuscript.

Written material: You may discuss this with your guides and key sources. Do not copy anyone else's paper, even if this is only imitation, otherwise it will be rejected on the grounds of plagiarism, which is illegal. Various methods to avoid plagiarism are strictly applied by us to every paper, and, if found guilty, you may be blacklisted, which could affect your career adversely. To guard yourself and others from possible illegal use, please do not permit anyone to use or even read your paper and file.

Criterion for Grading a Research Paper (Compilation) by Global Journals

Please note that following table is only a Grading of "Paper Compilation" and not on "Performed/Stated Research" whose grading solely depends on Individual Assigned Peer Reviewer and Editorial Board Member. These can be available only on request and after decision of Paper. This report will be the property of Global Journals.

Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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