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Highlights

A Study of the Psychotropic Activity

Effect on Glycemic Control in Patients

Pandemic Novel Coronavirus (Covid-19)

Evaluating Hydrocolloids of Sida Acuta

Discovering Thoughts, Inventing Future

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A Review: Pandemic Novel Coronavirus (COVID-19)

By Hariprasad M.G, Narayan Sah Sonar & Biki Ray

Abstract- The uncontrolled expansion of the novel coronavirus has stirred panic and unwelcoming sentiment and economic loss towards the world. The full spectrum of COVID-19 ranges from mild to severe respiratory illness with severe progressive pneumonia, multiorgan failure, and death. COVID-19 highly transmitted from person to person, thus need to the isolation of patients and maintain the quarantine. Lots of sought gain insights for vaccine design against SARS-CoV-2 (Severe Acute Respiratory Syndrome-Coronavirus-2) by considering the genetic similarities to SARS-CoV. This review article discusses the official updates on coronavirus, symptoms, transmission, diagnosis, reviews on pathogenesis, structure, treatment policy and our opinions on the use of drugs for the treatment of COVID-19 infection.

Keywords: *COVID-19, SARS-CoV-2, novel coronavirus, virus, wuhan, china.*

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A Review: Pandemic Novel Coronavirus (COVID-19)

Hariprasad M.G [α], Narayan Sah Sonar [σ] & Biki Ray [ρ]

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I. Introduction

Contagious diseases like from herpes and legionnaire's disease in the 1970s, to AIDS, Ebola, the SARS, and now COVID-19 continue to be dreadful and put pressure on human populations across the globe. Historians, who never lost enthusiasm for scourges, have a lot to offer[1].

SARS-CoV-2 is the reason for a continuous over the world outbreak of respiratory illness, known as coronavirus disease 2019 (COVID-19)[2].

It has confirmed that the virus is probably going to spread to most, if not all, nations. Regardless of terminology, this latest coronavirus disease is seeing increments in cases outside China[3]. The 2019 novel coronavirus epidemic, which was first reported in December 2019 in Wuhan, China, and has been pronounced a general wellbeing crisis of global concern by the World Health Organization, may advance to a pandemic related with substantial morbidity and mortality[4]. WHO has called the outbreak of SARS-CoV-2 infection as pandemic on 11 March 2020[3].

The chronology of COVID-19 diseases is as per the following. From December 18, 2019, through December 29, 2019, five patients were hospitalized with acute respiratory distress syndrome, and one of these patients died in Wuhan, China. On April 06, 2020, a total number of 1,285,257 positive cases among that 70,344 death cases reported. The COVID-19 is affecting 208 countries and territories around the world. (https://covid.worldometers.info/coronavirus/)

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II. Quarantine

Quarantine is defined as separation and restriction of movement of well persons presumed to have been exposed to contagion. "Isolation," in contrast, applies to the disunion of individuals who is known to be infected.

Even though, we are probably going to see more prominent utilization of vigorous social separating measures, such as school closures or the cancellation of public gatherings, broad sanitary cordons in which geographic areas were quarantined would bring up genuine protected issues. They also can present various logistical challenges and can expand the risk to those living in the restricted zone. Such measures may also have constrained adequacy with a highly contagious disease such as COVID-19.

At last, when governments confine individuals, they must meet those individuals' essential needs, ensuring access to social insurance, medication, food, and sanitation. Such standards wasn't constitutionally compelled: they are common to ensuring that detained persons agree to orders[5].

III. Symptoms

The most widely recognized symptoms at the onset of COVID-19 illness are fever, cough, and fatigue, while different manifestations include sputum production, headache, hemoptysis, diarrhea, dyspnoea, and lymphopenia.

Clinical highlights revealed by a chest CT scan introduced as pneumonia; in any case, there were abnormal signs such as RNAaemia, ARDS (Acute Respiratory Distress Syndrome), acute cardiac injury, and frequency of ground-glass opacities that led to death. At times, the multiple peripheral ground-glass opacities was observed in subpleural regions of both lungs that possible prompt both systemic and localized immune response that led to increased inflammation. Some of the cases shown an infiltrate in the upper lobe of the lungs that was related to increasing dyspnea with hypoxemia, through patients infected with COVID-19 developed gastrointestinal symptoms like diarrhea, a low percentage of MERS-CoV (Middle East Respiratory Syndrome-Coronavirus) or SARS-CoV patients experienced comparative GI distress[6].

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Table No. 1: The systemic and respiratory disorders caused by COVID-19.

Systemic Disorders	Respiratory Disorders
i. Fever	i. Rhinorrhoea
ii. Cough	ii. Sneezing
iii. Fatigue	iii. Sore throat
iv. Sputum Production	iv. Pneumonia
v. Headache	v. Ground-glass opacities
vi. Haemoptysis	vi. RNAemia
vii. Acute Cardiac injury	vii. Acute Respiratory Distress Syndrome
viii. Hypoxemia	
ix. Dyspnoea	
x. Lymphopenia	

IV. Transmission and Diagnosis

COVID-19 efficiently underwent replication in the upper respiratory tract and manifest a less abrupt onset of symptoms, the conventional human coronaviruses that are cause of common colds in the winter season. Virus undergoes replication in the upper respiratory tract and turn into large quantities during a prodrome period, are versatile, and carry on regular activities, adding to the spread of infection.

By contrast, transmission of SARS-CoV didn't promptly happen throughout the prodromal period when those infected, and most transmission was thought to have occurred when infected individuals presented with serious disease, thus possibly making it simple to contain the episodes SARS-CoV caused, unlike the recent outbreaks with COVID-19[7].

COVID-19 also exhibits affinity for cells in the lower respiratory tract and can undergo replication where, causing radiological confirmation of lower respiratory tract lesions in cases who don't present with clinical pneumonia. The clinical course of COVID-19 infection seems to have three patterns: mild illness with upper respiratory tract presenting symptoms; non-life-threatening pneumonia, and severe pneumonia with Acute Respiratory Distress Syndrome (ARDS) that begins with mild symptoms for 7–8 days[7].

It is understanding the implications of transmission of SARS-CoV-2 disease from persons with asymptomatic or very mild symptomatic cases of COVID-19 imperative for the plan of control strategies[8].

Currently COVID-19 appears to spread from individual to individual in a similar way as other common cold or influenza viruses i.e. face to face contact with a sneeze or cough, or from contact with secretions of individuals who are infected. The role of fecal-oral transmission in COVID-19 is not resolved yet. However, it was found to happen during the SARS outbreak[7].

Infectious droplets from sneezing, cough of the infected individual, and body fluids can easily contaminate the human conjunctival epithelium. Respiratory viruses are capable of inducing ocular respiratory infection. SARSCoV was dominantly transmitted through direct or indirect contact with mucous layers in the eyes, mouth, or nose of the infected individual. The fact that exposed mucous membranes and unprotected eyes expand the risk of SARSCoV transmission suggests that exposure of unprotected eyes to COVID-19 could cause acute respiratory infection[9].

The clinical attributes of COVID-19 pneumonia in pregnant women was similar to those reported for non-pregnant patients who developed COVID-19 pneumonia[10].

A COVID-19 is diagnosed by using reverse-transcriptase–polymerase chain reaction (RT-PCR) with primers and probes targeting the Orf1b and N genes of SARS-CoV-2.

The analysis proposes that the viral nucleic acid shedding example of patients infected with SARS-CoV-2 resembles patients with influenza and seems not quite the same as that found in patients infected with SARS-CoV. The viral load identified in the asymptomatic patient was like that in the symptomatic patients, which explain the transmission capability of asymptomatic or minimally symptomatic patients. These discoveries are similar with results that transmission might happen early in the course of infection and recommend that case detection and isolation may require strategies different from those need for the control of SARS-CoV[4].

V. Pathogenesis

Clinical and pathological discoveries in this critical case of COVID-19 cannot just assistance to determine a cause of death, but also gives new knowledge of the pathogenesis of SARS-CoV-2-related pneumonia, which might help physicians to formulate therapeutic strategy for similar patients and diminish mortality[11].

Patients with SARS had a triphasic pattern of illness.

The first phase of illness, patients most frequently initially presented with fever, a nonproductive cough, sore throat, and myalgia, with dyspnea regularly not turning into a noticeable feature until days 7–14 of the illness.

During the second phase of the illness, dyspnea and hypoxia, with continued fever and frequently accompanied by diarrhea, became more prominent. Some patient's respiratory status kept on disintegrating, and they developed ARDS required for mechanical respiration by the third week. The primary pathology observed at autopsy of patients that capitulated to contamination was diffuse alveolar damage.

The lungs of patients that died in the early phases of the infection contained hyaline membranes, edema, fibrin exudates, small vessel thrombi, loss and

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sloughing of pneumocytes, and a mixed cellular infiltrate of lymphocytes, macrophages, and polymorphonuclear leukocytes. Multinucleated giant cells that carried markers for macrophages and pneumocytes were often present.

At later phases of the disease, a histologic image of an organizing pneumonitis and consolidation, with type II pneumocyte hyperplasia, squamous metaplasia, and bronchiolitis obliterans was found. The relationship of worsening clinical progression with declining virus loads and the onset of an immunological response, in addition to the presence of markedly elevated cytokines levels, recommended that severe lung damage was largely immunopathological in nature[12].

VI. Structure of Virus

Coronaviruses were divided into three genera (alpha, beta and gamma coronavirus). Betacoronavirus demonstrated the potential for additional significant human diseases to result from coronavirus infections. For sure, soon after the identification of the SARS-associated human coronavirus (HCV)[12].

COVID-19 symbolize the seventh member of the coronavirus family that affects in humans and also categories under the orthocoronavirinae subfamily. The COVID-19 forms a clade inside the subgenus sarbecovirus. Given the genetic sequence identified and the phylogenetic reports, COVID-19 is sufficiently different from SARS-CoV, and it would thus considered as a new betacoronavirus that infects people. The COVID-19 probably developed from bat influence coronaviruses. Another counter of proof that supports the COVID-19 is of bat origin is the presence of a high level of homology of the Angiotensin-Converting-Enzyme-2 (ACE2) receptor from a variety of animal species, thus implicating these animal species as conceivable intermediate hosts or animal models for COVID-19 infections[6].

The "coronavirus" is coined from the Greek word for crown, as under electron microscope, the virus envelope shows like crowned shaped which characterized by ring of small bulbous structure[13].

Coronaviruses are enveloped viruses with round and sometimes pleiomorphic virions of approximately 80 to 120 nm in diameter. Coronaviruses contain positive-strand RNA, with the RNA genome about 30 kb. The genome RNA is complexed with the essential nucleocapsid (N) protein to shape a helical capsid found within the viral membrane. The membranes of all coronaviruses contain any of four viral proteins. These are:

i. Spike (S), the type I glycoprotein which forms the peplomers on the virus surface.
ii. The membrane (M) protein which transverse the membrane three times
iii. A short N-terminal a cytoplasmic tail and ectodomain, and
iv. A highly hydrophobic small membrane protein (E).

The E protein of IBV (Infectious Bronchitis Virus) has a short ectodomain, a transmembrane domain, and a cytoplasmic tail. The E protein of MHV (mouse hepatitis virus) was reported to transverse the layer twice, such that both N and C termini are on the inside of the virion. Some group II coronaviruses have an extra membrane protein, hemagglutinin esterase (HE). There is an additional group II virion protein called I for internal, as it was encoded within the nucleocapsid open reading frame (ORF) was a nonessential protein of unknown function. It has recently found that the ORF 3a-encoded SARS protein is an extra auxiliary protein. There might be other minor proteins, as yet undetected, included in virions.

The genomes of all coronaviruses have a comparable structure, about 20 to 22 kb carries the replicase gene, which encodes different enzymatic actions. The replicase gene products were encoded inside two broad open reading frames, ORFs 1a and 1b, which were translated into two polypeptides, pp1a and pp1ab, through a frame shifting mechanism involving a pseudoknot structure shaped by the genomic RNA. The basic proteins are encoded inside the three one-third of the genome, for all coronaviruses, in the order S-E-M-N. (When the HE protein was expressed, it is encoded 5 to S.) Each group of coronaviruses, in addition, encodes a group of unique small proteins; while these proteins are unnecessary and had been guessed to serve as accessory proteins and to interact or interfere with the host innate immune response, not shown for any of these proteins. The untranslated regions (UTRs) on either side of 5 and 3 ends of the genome, which were accepted to interact with the host and perhaps viral proteins to control RNA replication, which includes the synthesis of positive and negative strand genomic length RNA. Likewise, there are conserved sequences at the start of the transcription sites for each of the multiple subgenomic mRNAs; these are called transcriptional regulatory sequences (previously known as intergenic sequences). Coronavirus transcription was reviewed recently[13].

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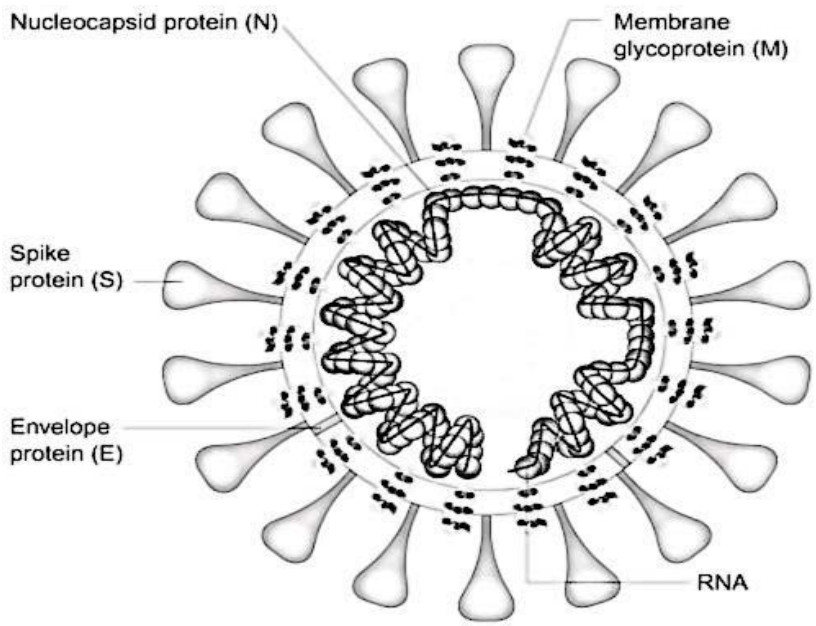


Fig. No. 1: Schematic diagram of the SARS coronavirus structure.

a) Structural Proteins of SARS-CoV-2 Are Genetically Similar to SARS-CoV

SARS-CoV-2 was observed to be near to SARS-CoV significantly more so than MERS-CoV based on full-length genome phylogenetic analysis, whether this is valid at the level of the individual structural proteins (S, E, M, and N). A direct reference arrangement based contrast indeed confirmed this, demonstrating that the M, N, and E proteins of SARS-CoV-2 and SARS-CoV had 90% genetic similarity, that of the S protein was prominently diminished (yet high). The resemblance between SARS-CoV-2 and MERS-CoV, then again, was significantly lower for all proteins, a feature that was also clear from the corresponding phylogenetic trees. We note that while the previous analysis was depend on the reference arrangement of each coronavirus, it was indeed a good representative of the virus, since less amino acid mutations was observed in the relating sequence data[14].

The percentage sequence identity with SARS-CoV-2 found as 76% S-protein, 96.6% N-protein, 91.1% M-protein, and 94.7% E-protein respectively compare with SARS-CoV[14].

VII. Treatment Policy

The first and most important is to isolate clinicians providing care from those making triage decisions. The "triage officer," upheld by a group with expertise in nursing and respiratory therapy, would settle resource allocation decisions and communicate them to the clinical group, the patient, and the family.

Second, these decisions should be inspected routinely by a centralized state-level monitoring committee.

Third, the triage calculation had been reviewed consistently as information about the infections evolves. If decision not to intubate patients with COVID-19 for more than ten days, for instance, then discovered that these patients need 15 days to recover, we would need to change our algorithms[15].

VIII. Treatment Options/ Therapeutics

The way of treatment included bi-daily oral administration of 75mg oseltamivir, 500mg lopinavir, 500mg ritonavir, and the intravenous administration of 0·25g ganciclovir for 3–14 days, another report indicated that the broad-spectrum antiviral remdesivir and chloroquine are exceptionally compelling in the control of COVID-19 infection. The National Medical Products Administration of China has approved the utilization of Favilavir, an antiviral drug, as a treatment for coronavirus.

However, lopinavir-ritonavir treatment did not significantly accelerate clinical improvement, reduce mortality, or diminish throat viral RNA perceptibility in patients with serious COVID-19. These information ought to advise future investigations to evaluate this and other medication in the treatment of infection with SARS-CoV-2. In this case of combining lopinavir–ritonavir with other antiviral agents, as has been done in SARS and is being studied in MERS-CoV, may upgrade antiviral effects and improve clinical outcomes remains to be determined[16].

There are considerable supporting the utilization of corticosteroids at a low-to-moderate doses in patients with coronavirus infection. According to the expert consensus statement, the accompanying essential standards ought to followed when utilizing corticosteroids:

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(1) The advantage and damage ought to have been carefully weighed before using corticosteroids;
(2) Corticosteroids ought to have been used prudently in critically ill patients with COVID-19 pneumonia;
(3) For patients with hypoxemia because of underlying diseases or who routinely use corticosteroids for chronic condition, further use of corticosteroids should be careful;
(4) The dosage ought to be low- to-moderate (≤0·5–1 mg/kg per day methylprednisolone or equivalent), and the duration ought to be short (≤7 days)[17].

IX. Novel Coronavirus Vaccines and Drugs

(https://Covid.clinicaltrialsarena.com/analysis/coronavirus-mers-cov-drugs/)

Table No. 2: Therapeutic and prophylactic approach for novel coronavirus

For all Vaccine and Drugs trail ongoing	
Novel Coronavirus Vaccine Approach	**Novel Coronavirus Drugs Approach**
a. Fusogenix DNA vaccine b. Gimsilumab, human monoclonal antibody c. AdCOVID, a single dose intranasal vaccine d. TJM2, a neutralising antibody e. Virus-Like Particles (VLP) by Medicago f. AT-100 (rhSP-D) a novel human recombinant protein g. TZLS-501 a monoclonal antibody h. BPI-002 to activate CD4+ helper T cells and CD8+ cytotoxic T cell i. Altimmune's intranasal coronavirus vaccine	a. OYA1, strong antiviral b. Remdesivir (GS-5734) c. Actemra d. Galidesivir (BCX4430) e. Regeneron f. SNG001, natural Interferon-β g. AmnioBoost for ARDS

X. Repurposed Drugs for Treatment of Covid-19 Infection

a) Artemether–Lumefantrine and Amantadine

In this article, we recommend and request for emergency use authorization for Co-artemether (Artemether–Lumefantrine) and amantadine for treatment of COVID-19 infection[18].

b) Local Antiseptic

Local antiseptic can wash of the throat infection of coronavirus, which further may prevent the SARS effects.

On going, German lab study supported by a manufacturer of povidone-iodine sore throat gargle, for instance, detailed that the solution was appeared to eliminate over 99 percent of the coronaviruses that cause SARS and MERS (very close cousins to the COVID-19). A prior Japanese lab study revealed that povidone-iodine products beat other antiseptics such as chlorhexidine gluconate and benzalkonium chloride in inactivating numerous other problematic viruses, such as coxsackie, rhinovirus, adenovirus, rotavirus, influenza. (https://COVID.nytimes.com/2020/03/29/well/live/gargle-gargling-coronavirus-infections-bacteria-virus.html)

XI. Conclusion

The transmission of COVID-19 can be preventing by, avoiding direct person to person contamination and maintaining well hygienic and sanitization. The research work for its diagnosis and treatment should bring out as soon as possible. Repositioning of drug efforts would be helpful in this emergency scenario as pharmacokinetics and pharmacodynamics of the drug are known.

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A Study of the Psychotropic Activity of Extracts of *Hedysarum Alpinum* L. and *Garcinia Mangostana* L

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Abstract- *Introduction:* The present research featured extracts of *Hedysarum alpinum* L. and *Garcinia mangostana* L. The extract of *Hedysarum alpinum* L. proved to have a more pronounced effect on the dopamine-induced changes in animal behavior in an active avoidance conditioning model as compared with such popular antipsychotic drug as haloperidol.

Methodology: The antipsychotic effect was evaluated based on active avoidance conditioning model in a two-compartment shuttle chamber. The anti-anxiety effect was evaluated in terms of passive avoidance conditioning. The side depressive effect of the extracts was evaluated based on the behavior of the animals during the Open Field test.

Keywords: *Hedysarum alpinum L., Garcinia mangostana L., active avoidance conditioning, passive avoidance conditioning, open field test, antipsychotic effect, anti-anxiety activity.*

GJMR-B Classification: *NLMC Code: QV 752*



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A Study of the Psychotropic Activity of Extracts of *Hedysarum Alpinum* L. and *Garcinia Mangostana* L

Fedorova Yu.S. [α], Kulpin P.V. [σ], Suslov N.I. [ρ], Denisova S.V. [ω], Tretyak V.M. [¥], Merkuryeva A.G. [§], Beregovykh G.V. [χ], Barkin I.M. [ν] & Lyamin E.S. [θ]

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Results: The test animals treated with *Hedysarum alpinum* L. extract demonstrated no significant change in the orientation and investigative behavior. The animals in the control group were given haloperidol, which appeared to have a distinctive inhibitory effect. The test animals in the *passive avoidance conditioning model* demonstrated a lower level of cognitive impairment under the influence of the pericarp extract of *Garcinia mangostana* L. This result can be associated with its positive effect on the emotional status, which plays an important role in memory trace formation. Phenazepam, on the contrary, had a negative effect on the formation and reproducibility of conditioned reflexes of aversive factor avoidance. The test group treated with *Garcinia mangostana* L. extract also showed no significant change in the orientation and investigative behavior compared to the control group.

Conclusion: Therefore, the extract of *Hedysarum alpinum* L. proved antipsychotic while causing no depressing effect. Thus, the extract of *Garcinia mangostana* L. possessed anti-anxiety activity and produced no depressing effect.

Keywords: Hedysarum alpinum L., Garcinia mangostana L., active avoidance conditioning, passive avoidance conditioning, open field test, antipsychotic effect, anti-anxiety activity.

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I. Introduction

Bad environmental conditions and stressful social situations increase the risk of neuropsychiatric disorders. As a result, neurotropic drugs, e.g. anxiolytics, antipsychotics, and psychostimulants, are becoming more and more marketable. Chlorpromazine was the first antipsychotic drug (1951) [7]. It was followed by anxiolytic drugs, e.g. diazepam, which appeared in 1963 [10]. These drugs marked the beginning of the psychopharmacology era. From then on, medical science has been striving to develop such a natural substitute for chemical medicinal products that would maintain pronounced therapeutic properties and produce no side effects.

Based on the neurobiological theory of consciousness, F. Crick, K. Koch [6], S. Gershon, and A. Eison defined the main properties of the “ideal” tranquilizer, or anxiolytic agent. First of all, it should possess a pronounced therapeutic effect, i.e. selective reduction of anxiety, and be innocuous. Second, it should not inhibit psychomotor functions, cognitive activity, attention, and memory. Finally, an ideal tranquilizer is non-toxic and does not aggravate the depressing side effects caused by other drugs [4].

As for the optimal spectrum of pharmacological activity, an “ideal” antipsychotic should be able to reduce positive symptoms, improve cognitive functioning, prolong remission, and prevent relapse. These properties should be combined with the highest possible level of innocuousness and no depressing effect [5].

Unfortunately, modern medicine possesses no psychotropic drugs that fully comply with the above criteria. Therefore, a search for phytogenic drugs with antipsychotic and anxiolytic properties remains relevant.

Chemical medicinal products currently used to treat mental disorders have a depressing effect. As a result, they produce a number of side effects, which

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limits the possibility of their use, especially for patients whose work is associated with a longer-term attention span. Many antipsychotic drugs also produce a negative effect on cardiac activity, cause hyperprolactinemia (increased secretion of prolactin), suppress growth hormone, and trigger obesity and malignant antipsychotic syndrome [2].

Several Russian and foreign studies revealed psychostimulating, sedative, and anticonvulsant properties in plants of the *Hedysarum* and *Garcinia* genera [3, 8]. However, *Hedysarum* and *Garcinia* extracts proved to lack some of the side effects typical of chemical medicinal products. For instance, they did not produce the inhibitory effect that anxiolytics and anticonvulsants are known to have.

New drugs based on *Hedysarum* and *Garcinia* extracts will be efficient and without side effects. Therefore, their development is an urgent task, since they will be able to significantly improve the quality of life of patients during pharmacotherapy. However, while the chemical composition of these extracts received much scientific attention, their pharmacological properties remain largely understudied.

A study into the effect they produce on the cognitive functions and dopaminergic system seems to have a high scientific and practical potential. In this regard, passive and active avoidance conditioning tests can be especially informative. These tests make it possible to evaluate the effect of *Hedysarum* and *Garcinia* extracts on cognitive processes and predict their antipsychotic and anti-anxiety properties.

II. Materials and Methods

The present research featured dried 95% aqueous alcoholic tinctures of pericarp of *Garcinia mangostana* L. and aerial parts of *Hedysarum alpinum* L.

A set of experiments revealed the effect of the plant extracts on active avoidance conditioning, as well as orientation and investigative behavior of male Wistar rats during Open Field tests. Passive avoidance conditioning tests featured BALB\C male mice. All test animals were found conventional and of the first category. They were obtained from the Department of Experimental Biological Models of the E.D. Goldberg Research Institute of Pharmacology and Regenerative Medicine (Tomsk National Research Medical Center of the Russian Academy of Sciences, Tomsk, Russia). The tests were performed from 9am to 15pm. The animals were kept under standard vivarium conditions. They followed a standard feeding diet in accordance with the rules adopted by the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (Strasbourg, 1986).

The test samples were dissolved in purified water and administered to the animals intragastrically. The dose was 200 mg per 1 kg of body weight. The intact control group received purified water. The doses of haloperidol and phenazepam were 2 mg per 1 kg of body weight. These drugs were dissolved in purified water and used as comparators.

The antipsychotic effect was evaluated based on active avoidance conditioning model in a two-compartment shuttle chamber. The active avoidance conditioning lasted 2 days. The first session included 50 representations. The second session was conducted a day later and included 20 runs. One hour after it was administered the test sample or water (in the control group), the rat was placed in the first compartment. A sound signal followed 20 seconds later. Immediately, a light came on in the safe compartment. It served as the conditioned stimulus. The sound signal was followed by a 10-second delay-of-reward period. After that, an unconditioned stimulus in the form of impulse current was applied to compartment where the rat was sitting. The frequency was 5 pulses per second, while the amplitude slightly exceeded the threshold value and equaled 20-45V.

The threshold current values were defined individually. They were based on the animal's reaction marked with the start of squeaking. If the rat did not run into the illuminated safe compartment after the delay-of-reward period, it was given a series of electric shocks which persisted until the animal entered the safe compartment. The rat remained in the safe compartment for 15-90 seconds. The intervals were randomized to prevent habituation. After that, the procedure was repeated. The reaction was considered correct if the rat ran into the safe compartment before 10-second delay-of-reward period elapsed. The reflex was considered stable after nine out of ten consecutive correct reactions to the conditioned signal. The drug effect was evaluated in comparison with the control groups. The analysis also included interstimulus runs, i.e. switching compartments before the sound conditional signal [1].

The anti-anxiety effect was evaluated in terms of passive avoidance conditioning. The conditioning was conducted in a chamber that consisted of one large illuminated compartment and one small dark compartment. The animal was placed in the illuminated compartment. Due to the congenital preference for dark, it took the animal 10-20 seconds to move into the small dark compartment. After that, the door between the two compartments was closed. The floor of the dark compartment contained parallel alternating electrodes. When the animal was in, it was given electric current pulses. Each pulse lasted 50 msec with a frequency of 5 Hz and amplitude of 50 mA. After 10 sec, the door was opened and the animal was allowed to move into the safe illuminated compartment. As a result, the animal developed a conditioned reflex of dark space avoiding. To check the reproducibility, the animal was placed in the illuminated compartment in the corner opposite to

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the door to the dark compartment and observed for three minutes. The experiment registered the time of the first entry into the dark compartment, i.e. the latent time of entry, and the total time spent in the dark compartment. The reflex was considered stable if the animal did not venture into the dark compartment for three minutes, or if the latent time exceeded 150 sec. The quality of the reflex was assessed according to the share of the animals that developed it. The experiment included several additional indicators that described the conditioned reflex and behavioral status, i.e. the number of entries into the dark compartment, the time spent in the dark compartment, and partial entry into the dark compartment [1].

The side depressive effect of the extracts was evaluated based on the behavior of the animals during the Open Field test [9]. The degree of the depressive effect depended on the degree of inhibition of investigative activity. The Open Field test was performed in a chamber of 100x100x40 cm with white walls. Its floor was divided into 16 squares. Each square had a circular hole (3 cm in diameter). The chamber was illuminated by an electric incandescent lamp with a 100-watt light bulb placed 1 m above the floor. The rat was put in a corner and observed for three minutes. There were two check-lists: one for the first minute and one for the two remaining minutes. The check-list registered the number of movements from square to square (horizontal activity), the times the animal stood on its hind legs (vertical activity), sniffing and hole exploration (hole exploratory behavior), washing (grooming), and bowel movements (number of droppings). The skewness ratio in the behavior (%) was calculated as the ratio of the number of horizontal movements vs. the total physical activity. The results of the first minute and two subsequent minutes of testing were evaluated separately and together.

III. Results and Discussion

The active avoidance conditioning was successful in the control rats. The animals demonstrated the reflex after 24 hours (Fig. 1).

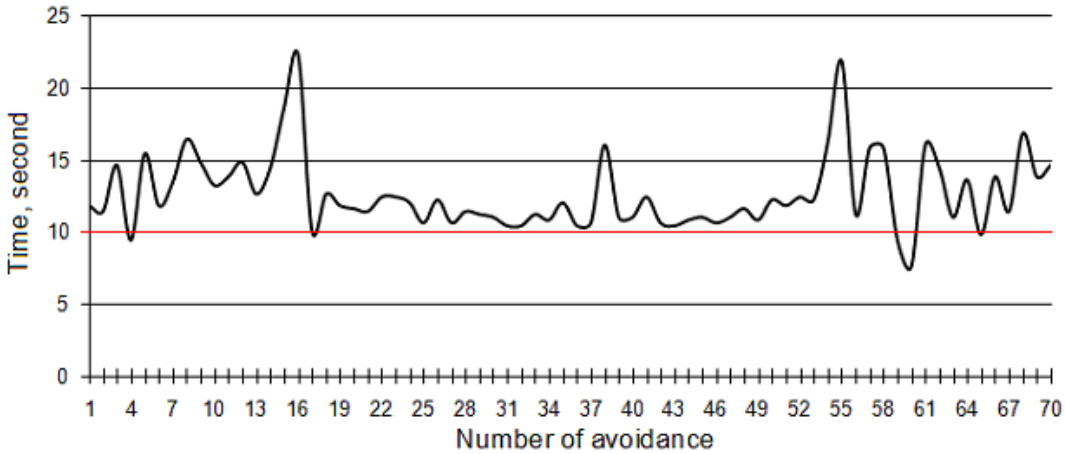


Fig. 1: Acquisition of the Active Avoidance Conditioned Reflex in the control group

After administration of haloperidol, the animals did not avoid the electric pain stimulus and demonstrated a longer latency period when moving to the dark compartment (Fig. 2).

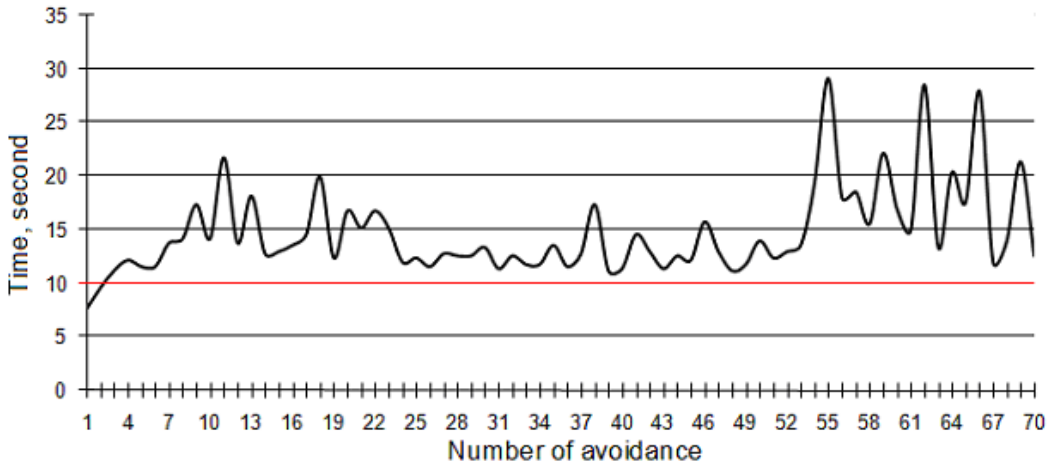


Fig. 2: The Effects of Haloperidol on Acquisition of the Active Avoidance Conditioned Reflex

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The active avoidance conditioning resulted in a significant increase in the latency period that preceded the entry into the dark compartment in the animals treated with the *Hedysarum alpinum L.* extract compared with the control group and the comparison group where the animals were given haloperidol as a common antipsychotic (Fig. 3).

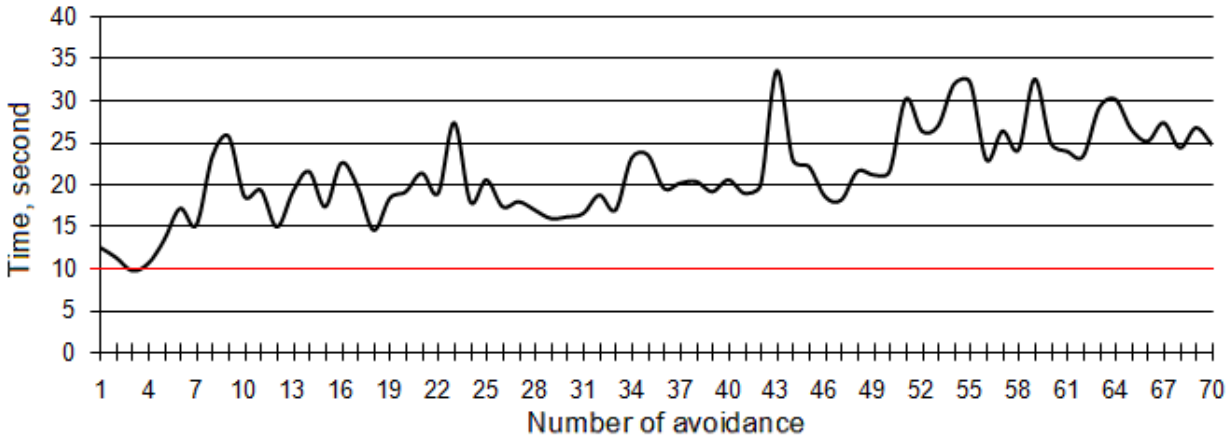


Fig. 3: The effect of herb extract of *Hedysarum alpinum* L. on Acquisition of the Active Avoidance Conditioned Reflex

Thus, the extract of *Hedysarum alpinum L.* proved to have a more pronounced effect on dopamine-induced changes in animal behavior compared to such popular antipsychotic as haloperidol.

The animals treated with the pericarp extract of *Garcinia mangostana* L. demonstrated a significantly lower ability to develop active avoidance reflex, compared with the control group. The animals did not avoid electrical impulses and moved to the safe compartment immediately after being exposed to electricity, while the function of reward prediction had obviously been affected (Fig. 4).

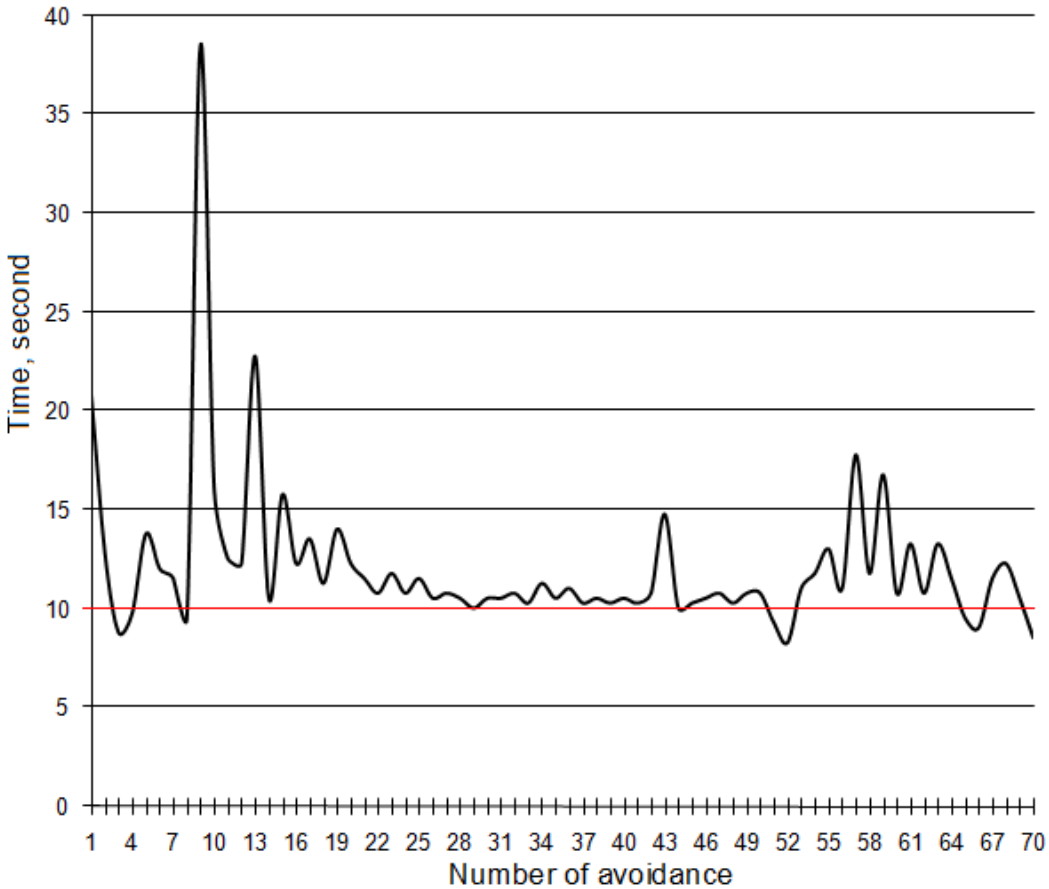


Fig. 4: The effect of pericarp extract of *Garcinia mangostana* L. on Acquisition of the Active Avoidance Conditioned Reflex

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After administering the pericarp extract of *Garcinia mangostana* L., the depressed activity in the system of goal achievement was accompanied by a lower level of neurotic resistance. These effects may be due to the fact that the pericarp extract of *Garcinia mangostana* L. blocks postsynaptic receptors and thereby disrupts dopaminergic transmission of nerve impulses in various parts of the central nervous system.

The processes of development and reproduction of conditioned passive avoidance reflex is the most common experimental technique used to study memory, as well as the development and stability of conditioned reflexes. In this case, the behavioral essence of the reflex is a conflict between the congenital-to-rodents reflex of dark space preference and the acquired conditioned reflex of avoiding the electric pain stimulus inflicted in this dark space during conditioning. Table 1 shows the effect of plant extracts on passive avoidance conditioning.

Table 1: The effect of plant extracts on Acquisition of the Passive Avoidance Conditioned Reflex

Group	Conditioning	24 h			7 days		
	1 entry, sec	1 entry, sec	Number of entries	Time spent in the dark compartment, sec	1 entry, sec	Number of entries	Time spent in the dark compart-ment, sec
Control group	15.6± 2.61	161.9± 9.55	0.6± 0.27	4.5± 2.11	138± 17.05	0.9± 0.4	8.2± 4.86
Phenazepa-mum	54.9*± 21.12	130.3*± 22.42	1.1*± 0.48	38.1*± 19.78	147.7*± 21.56	0.3*± 0.21	31.6*± 21.08
Extract of *Hedysarum alpinum* L.	34.1*± 17.4	133*± 17.13	1.7*± 0.54	23.1*± 10.42	122.7*± 19.5	2.0*± 0.7	19.9*± 6.15
Extract of *Garcinia mangostana* L.	26.1*± 2.9	150.9± 13.9	1.5*± 0.33	12.5*± 5.6	141.3± 16.19	1.1± 0.48	12*± 5.53

*Notes: Controls received distilled water; the number of animals in each group was n = 10 (total number of animals = 40); *p < 0.05.*

The animals that were given extracts of *Hedysarum alpinum* L. and *Garcinia mangostana* L. had a larger number of entries into the dark compartment, while the time they spent there decreased, compared with the group of animals treated with phenazepam. Not only do animals under stress demonstrate an anxiodepressive state, but they also show a definite decline of cognitive function. The animals treated with phenazepam demonstrated a pronounced cognitive impairment, i.e. the latent period of the first entry into the dark compartment decreased while the number of entries increased. Moreover, the animals treated with phenazepam were more depressed: they spent more time in the dark compartment. The animals treated with *Garcinia mangostana* L. extract and, to a lesser extent, those treated with the extract of *Hedysarum alpinum* L., showed better learning skills and memory during the test. The animals treated with the pericarp extract of *Garcinia mangostana* L. proved to have the most stable reflex.

The lower cognitive impairment in the animals treated with *Garcinia mangostana* L. may be associated with the positive effect the extract has on the emotional status, which contributes to better memory trace formation. As for phenazepam, it had a negative effect on the development and reproducibility of conditioned reflexes of aversive factor avoidance. The Open Field test provides a typical acute stress environment (stress of novelty), accompanied by adaptation to new conditions. Novelty stress generalizes exaltation and increases anxiety. When placed in unfamiliar environment, the animal activates behavior due to its natural curiosity, which is an unconditioned self-development reflex. This activation is intensified by anxiety, i.e. fear, or stress, of novelty. The system of behavioral inhibition manifests itself through anxiety. Its main function is to monitor the success of current activities. In the Open Field environment, the system of behavioral inhibition has an ambivalent effect on behavior indicators: the high level of anxiety suppresses investigative activity, while its low or medium level activates the behavior Fig. 5 illustrates the orientation and investigative behavior under the Open Field conditions.

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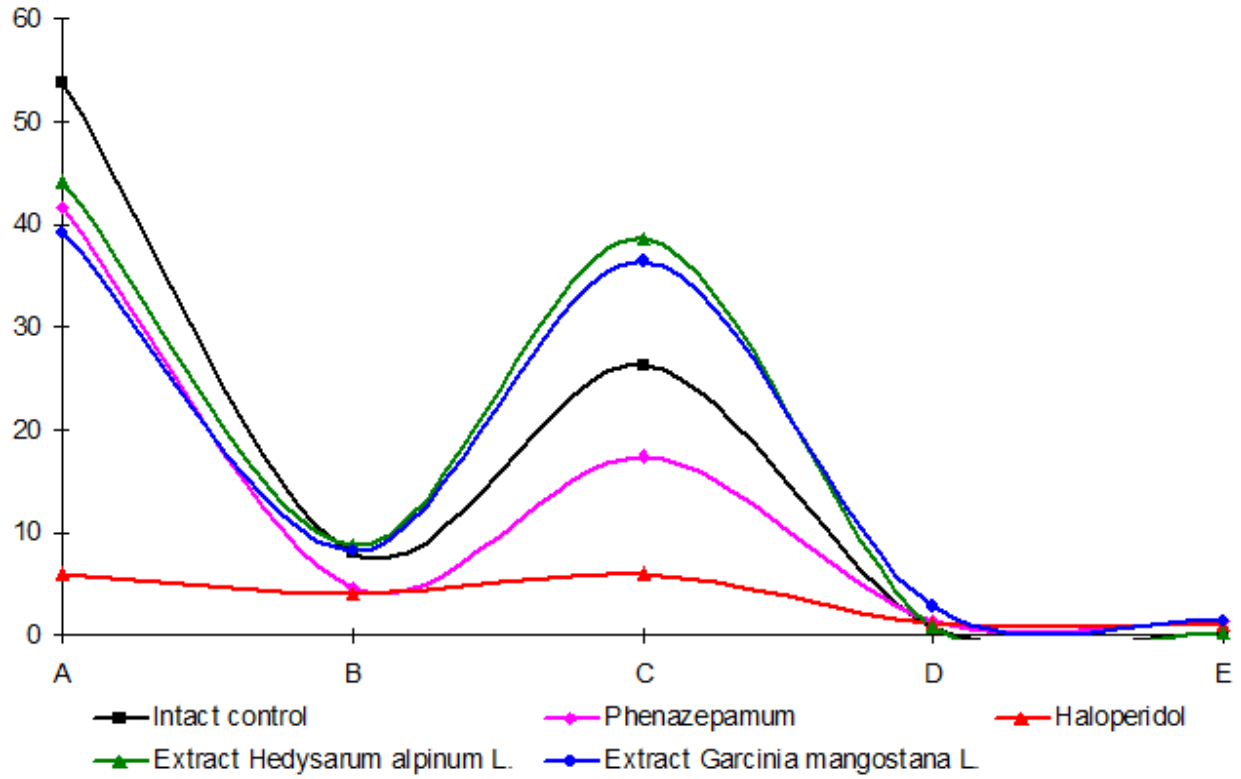


Fig. 5: Effect of plant extracts on the approximate research behavior of mice in the open field test: A - Horizontal activity (number of times the line of a square is crossed with all 4 legs); B - Vertical activity (number of times the animal stands on its hind legs); C - Research reflex (number of peeping and sniffing holes); D - Grooming (frequency of grooming activity); E - Defecation (number of defecation boli)

The animals treated with haloperidol clearly experienced its inhibitory effect on orientation and investigative behavior. The animals treated with phenazepam also demonstrated a lower orientation and investigative activity, compared with the control group, but not as low as in the haloperidol group.

The extract of *Hedysarum alpinum* L. and the pericarp extract of *Garcinia mangostana* L. lowered the horizontal activity index and boosted the investigative activity index, compared with the control group. The research revealed no depressing effect in the plant extracts of *Hedysarum alpinum* L. and *Garcinia mangostana* L.

IV. Conclusion

The experiment proved that the extract of aerial parts of *Hedysarum alpinum* L. had antipsychotic properties while showing no depressing effect. The pericarp extract of *Garcinia mangostana* L. improved the conditioned reflex activity in the test animals after passive avoidance conditioning, which also indicates antianxiety activity and no depressing effect.

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Evaluating Hydrocolloids of *Sida Acuta* as Sustained Release Matrix for Ibuprofen Tablet

By Akpabio E I, Uwah T O, Effiong D E & Godwin J

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Abstract- Background and Objectives: Matrix tablet formulation for ibuprofen using natural hydrocolloids are a good alternative to conventional ibuprofen immediate-release tablet and would be a desired option as opposed to the use of synthetic polymer. This work was to prepare and evaluate sustained-release ibuprofen matrix tablets using *Sida acuta* gum. Guar gum is the reference natural polymer.

Materials and Methods: Sida gum was obtained from aqueous macerate of *Sida acuta* leaves then precipitated using acetone, whereas guar gum was purchased. Both gums were characterized for micromeritics, swelling properties, and hydration capacities. The granules of ibuprofen, using a gum for a separate batch, were prepared by wet granulation method. The matrix tablets were produced, physical properties determined, and dissolution studies carried out. The release kinetics values obtained were fit into equations for kinetic studies.

Keywords: Sida acuta gum, ibuprofen, sustained release, matrix tablet, guar gum.

GJMR-B Classification: NLMC Code: QV 745



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Evaluating Hydrocolloids of *Sida Acuta* as Sustained Release Matrix for Ibuprofen Tablet

Sustained Release Ibuprofen Tablet using *Sida Acuta* Gum

Akpabio E I [α], Uwah T O [σ], Effiong D E [ρ] & Godwin J [ω]

Abstract- Background and Objectives: Matrix tablet formulation for ibuprofen using natural hydrocolloids are a good alternative to conventional ibuprofen immediate-release tablet and would be a desired option as opposed to the use of synthetic polymer. This work was to prepare and evaluate sustained-release ibuprofen matrix tablets using *Sida acuta* gum. Guar gum is the reference natural polymer.

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Results: Ibuprofen granules using guar gum (G1) had a flow rate of 5.19 g/s and particle density of 1.22 g/ml while granules containing *Sida acuta* gum (G2) had a flow rate of 5.60 g/s, granule and particle density of 1.23 g/ml. Tablets for both batches complied with official standards in mechanical properties of friability and crushing strength. The release kinetics obtained from the *in vitro* dissolution study showed that Batch G1 released 94.55 % of the ibuprofen while Batch G2 released 96.82 % of it in the 8 hours. Both batches followed zero-order while the mechanism of release was non-Fickian diffusion as the n-diffusion exponent was less than 0.5 for both batches. The t-test showed significant difference in the percentage of drug released by both batches of tablets ($P < 0.05$).

Conclusion: Sida acuta gum was useful as the sustained-release delivery of ibuprofen as the matrix tablets gave out higher content of the therapeutic active ingredient hence could serve as a substitute for synthetic polymer in drug delivery.

Keywords: Sida acuta gum, ibuprofen, sustained release, matrix tablet, guar gum.

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I. Introduction

The non-invasiveness, convenience, and ease of administration that characterize the oral route make it the route of choice in drug use. Solid dosage form drug design and presentation (which uses the oral route) continues to be improved upon to achieve reduced dosage frequency, better patient compliance, and, more importantly, improved therapeutic efficacy. This tripartite intention of drug formulation is achievable when drugs are delivered at non-toxic steady state in the plasma or the tissue level despite changing the *in-vivo* environment[1]. Despite the many synonyms used to explain delivery strategies that maintain plasma steady-state, sustained-release (SR) is one of such nomenclatures that accurately describe drug delivery systems that help to achieve these intentions by continuously releasing the therapeutic actives over an extended period on single dosing, thereby maintaining a prolonged effect. Orals, injectibles, and topicals have been formulated as sustained delivery. Some approaches employed to arrive at sustained release include; encapsulation of slow-release granules, tableted slow release granules, drug complexation technique, coated tablets, ion activated system, and even the tablet matrix system [1,2]

In the matrix system, a therapeutic active is embedded throughout the polymer matrix of insoluble/hydrophilic substance. The release of the drug depends on drug dissolution within the polymer matrix and diffusing out through pores in the matrix. In some formulations, the matrix physically increases in size to form a gel as the drug dissolves in it, thus allowing the drug to exit through the gel's outer surface. Many naturally occurring polymers with unique, desirable drug release retarding characteristics are used in filling the roles of excipients for SR. For the matrix systems, polymers in use include starches, hydrocolloids and cellulose as well as their derivatives. The use of gums in dosage forms and in formulating sustained release are reported in the literature. [3,4,5,6]

Sida acuta (SA) is a weed of tropical, semi-avid, and occasionally sub-tropical and warmer temperate regions. It invades open woodlands, pastures, waterways (i.e., riparian vegetation) plantations, crops, and gardens. The whole plant, although smoked in

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Mexico as a substitute to Marihuana, is reported to being widely used as a traditional medicine in Columbia, especially as an external bath for snake bite [7]. The leaves of the plant are the source of the hydrocolloid used in this research work.

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) used for treating pain, fever and inflammation. Some of the conditions it covers include dysmenorrhea, migraines, and rheumatoid arthritis. It has been used with some success for treating ankylosing spondylitis, gout, and psoriatic arthritis. It may reduce pain, fever, and inflammation of pericarditis. The need for managing recurrent chronic pain while overcoming frequency of administration, especially for drugs with short half-life, has necessitated the production of analgesics with sustained-release. One of such is the Neurofen® 300mg back pain capsules (an encapsulated slow-release pellet of ibuprofen). This work, therefore, was to design, formulate and evaluate sustained-release ibuprofen matrix tablets using *Sida acuta* hydrocolloid as the matrix former. Guar gum was used as a reference natural polymer.

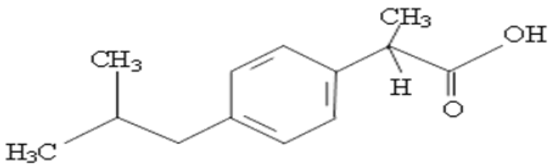


Fig. 1: Chemical structure of Ibuprofen

II. Materials and Methods

Ibuprofen hydrochloride, guar gum (Riedel De Haenac Seelze Hannover) and Microcrystalline cellulose (Guarajat Micro wax Limited, India) were obtained commercially whereas the *Sida acuta* gum was obtained locally from the leaves of the plant (from Faculty of Pharmacy farm, University of Uyo, Nigeria).

a) Study area

The study was carried out in the Undergraduate Pharmaceutics laboratory, instrument room for dosage form evaluation, and the tableting unit, all of the department of Pharmaceutics, Faculty of Pharmacy, University of Uyo, Nigeria from November 2018 - April 2019.

b) Preparation of Sida acuta gum

The leaves of the *Sida acuta* plant were collected, milled into small sizes, and weighed. The milled leaves were macerated in 7 L of hot water containing 0.1% of sodium metabisulphite for 24 h. After that, the macerate was filtered. To the filtrate, an equal volume of acetone was added in order to precipitate the gum. The precipitate was further washed with acetone severally to remove the chlorophyll and then air-dried for 24 h. The dried gum was weighed and evaluated.

c) Evaluation of the gum

The solubility, swelling index, water absorption index, pH, and organoleptic features of the gum were determined as described in previous researches [4,8]

d) Swelling Index

About 1.0 g quantity of SA gum was weighed into a measuring cylinder, and the volume occupied noted. Distilled water (10 mL) was added to it, shaken vigorously, and allowed to stand for 24 h. The supernatant was subsequently decanted but the volume of the sediment noted. The test was carried out in triplicate. The swelling index was calculated using the relation:

$$S = \frac{V2}{V1}$$

Where S = Swelling index

V1 = Gum volume before hydration

V2 = Gum volume after hydration

This test was also carried out for the guar gum.

e) Solubility Test

The solubility of gum was evaluated three solvents: water, ethanol and acetone. A 1g quantity of gum was weighed and placed in a clean test tube to which 10 mL of distilled water was added. The mixture was shaken vigorously and observed for formation of a homogenous phase. This same procedure was also carried out using the other solvents.

f) Water Absorption Index

A 1 g quantity of gum was weighed into a dish of known weight, and spread to cover the base of the dish. Water was filled in a bucket to a certain level to allow the petri dishes be placed, floating on the water in the bucket. The bucket was covered and allowed to stand for 24 hours, after which the petri dishes were, removed, wiped off, and re-weighed. This procedure was repeated for 48 hours, 72 hours and 96 hours, respectively. The percentage increase in weight, taken as the water absorption index was calculated. Determinations were done in triplicates.

g) pH Test

A 1% w/v dispersion of the gum in water was prepared and the pH determined using a bench-top pH meter (Thermo Scientific Orion Versa star). pH determinations were made in triplicate and the mean value, determined.

h) Preparation of Granules

Two batches of granules were prepared. A gum was used in each batch as the matrix-forming agent. The granules were prepared by the wet granulation technique. The ingredients were weighed accurately and properly mixed in a porcelain mortar. The weighed

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powdered mix was formed into a damp mass for granules production using 95% ethanol. The wet mass was screened through a 2 mm stainless steel sieve and the resulting granules dried at 60°C in a hot air oven (P Selecta, Spain) for 1 hour. The dried granules were further screened, using 1mm stainless steel sieve, and stored for further evaluations.

Table 1: The composition of Ibuprofen-Matrix tablet

Ingredients	G1	G2
Ibuprofen (mg)	200	200
Guar gum (%)	20	-
Sida acuta gum (%)	-	20
Magnesium stearate (%)	1	1
Talc (%)	1	1
MCC q.s to	400mg	400mg

i) Evaluation of Granules

The flow rate, angle of repose, bulk density, tapped density, Hausner's quotient, and Carr's compressibility index were determined in line with methods described by Akpabio*et al*.,(2016) [4] using 30 g of the granules.

i. *Granule density and Porosity*

The fluid displacement method was employed for determination. The weight of a 50 ml pycnometer was determined and noted. After that, the pycnometer bottle was filled with xylene and the excess wiped off. The filled bottle was re-weighed and the difference between this new weight and the empty pycnometer bottle was calculated. A 0.5 g quantity of granules was transferred into the pycnometer bottle. The excess xylene displaced by the granules was wiped off, the bottle further re-weighed. The granule density was calculated using the equation below.

$$\text{Granule density } \rho g = \frac{\rho(Ws)}{Ws-(W2-W1)}$$

G Where

ρ = density of xylene, Ws= weight of sample (granules),
W_2 = weight of pycnometer + xylene + sample
W_1 = weight of pycnometer + xylene

$$Granule\ porosity(\varepsilon)\frac{100(1-\rho b)}{\rho g}$$

Where

ρb = bulk density, and ρg = granule density

j) Formulation of Ibuprofen matrix tablets

The dried granules of ibuprofen were further sieved using a 0.25 mm stainless steel sieve to separate the fine granules from the coarse granules. The weight of the fine granules was determined and the percentage fines were calculated. The fine granules were mixed with magnesium stearate in a beaker and the coarse granules were also incorporated in the beaker and mixed properly. Talc was weighed and added to the mixture of granules and magnesium stearate, and the mixture was compressed at 25 KN using a single punch tableting machine (Cadmach Machinery Co. Pvt Ltd, India).

k) Evaluation of Physical Properties of the Tablets

i. *Tablet Diameter and Thickness*

Ten tablets from each of the batches were selected at random and the diameter and thickness of each tablet was determined using the micrometer screw gauge. The average values of the parameters for each batch was then calculated.

ii. *Tablet Weight Uniformity*

Twenty tablets were randomly selected from each batch, weighed individually, and the average weight was determined using an electronic scale (Ohaus Corporation, Australia). The mean and percentage variation was calculated for each batch.

iii. *Tablet Hardness and Friability*

This was done using the hardness tester. Ten tablets were chosen at random from each batch. Each tablet was placed diametrically between the Monsanto hardness tester (Rolex, Chandigarh), and the force needed just to crush the tablet was noted. The mean of the hardness of each batch was determined. Another ten tablets from each batch were obtained dusted, weighed and placed in separate drums of a Roche friabilator (DT-2D). The tablets were tumbled at a speed of 25 revolutions per minute for 4 minutes. The tablets were then removed, dusted and weighed again. The friability of the tablets were expressed as a percentage using the formula below;

$$\text{Friability} = \frac{change\ in\ tablet\ weight}{original\ \ tablet\ \ weight} \times 100$$

iv. *Preparation of Ibuprofen Standard Calibration Curve*

The standard concentration was prepared by dissolving 50 mg of Ibuprofen in 50 mL of 95% ethanol. This stock concentration was serially diluted appropriately using 0.1N HCl. The drug was assayed with a spectrophotometer (U2100 PC Shanghai, China) and a standard curve of absorbance versus concentration was determined.

v. *The in vitro Drug Release Study of Ibuprofen Sustained Release Tablet*

The in vitro dissolution study for the tablets was carried out using the USP basket method at 50 rpm (revolutions per minute) in a 900 mL dissolution medium containing 0.1NHCl maintained at 37 ± 0.5. A 10 mL aliquot were withdrawn and replaced with an equivalent 10 mL of the fresh dissolution medium. The withdrawn aliquot was filtered through a Whatman filter paper, and assayed using the UV Spectrophotometer (U2100 PC Shanghai, China). The assay was done at a wavelength of 264 nm.

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vi. *Tablet Content Uniformity*

Three tablets from each batch were weighed and crushed. The powder was mixed with 20 mL of chloroform for 15 minutes and filtered. The residue was then washed with three 10 mL of chloroform and the combined filtrate was gently evaporated to dryness. The residue from the filtrate was dissolved in 50 mL of methanol (95%). This solution of the residue in methanol was titrated using 0.1M sodium hydroxide solution, and an indicator, phenolphthalein. The content of ibuprofen was calculated with each milliliter of 0.1M sodium hydroxide equivalent to 0.02063 g of Ibuprofen.

III. Results and Discussion

a) Results

i. *Properties of Gums*

The leaves of *Sida acuta* yielded a 3.75% gum and is used at a concentration of 20% as a matrix former in this formulation (table 1). The yield of the gum from the leaves is low. The *Sida acuta* gum is a dark brown gum with a characteristic smell. On standing in an aqueous medium, it gave a swelling power of about 8%, and the dispersed gum in the aqueous medium is slightly acidic. Other physicochemical properties of the gum are given in Table 2. The Ruthenium and Molisch test carried out on *Sida acuta* gum gave results found in Table 3. The results confirmed that what was obtained after preparation from the leaves is the hydrocolloid.

Table 2: Properties of Guar Gum and *Sida acuta* Gum

Parameters	Guar Gum	*Sida acuta*
Organoleptic properties	Off white odorless substance	Dark brown with a characteristic odor
Swelling index	8.64 ± 0.12	8.36 ± 0.15
pH	6.06 ± 0.10	5.88 ± 0.21
Water absorption index	1.28 ± 0.13	1.26 ± 0.17
Solubility		
In water	Soluble to form mucilage	Slightly soluble
In ethanol	Insoluble	Insoluble
In acetone	Insoluble	Insoluble

Table 3: Confirmatory Tests of Gum

Test	Observation	Inference
Ruthenium Test: Small quantity of dried gum powder mounted on a slide with ruthenium red solution and observed under a microscope	Pink color develops in both samples	Gum present
Molisch test : 0.1g of dried gum powder + Molisch's reagent + conc. H_2SO_4 on the side of the test tube	Violet color observed at the function of the two layers in both samples	Carbohydrate present

b) Micromeritics of Granules and Properties of Tablets

The densities, Carr's index, and other micromeritic parameters of both batches of granules are represented in the Table 4 below. The micromeritics of powdered materials is a measure of the flow property and indicates the potential for use in direct compression. The batch of granules formed from the gum had good flow properties with the Hausner's quotient and Carr's index being < 1.2 and 12% respectively. This means granules formed from the gum can be compressed without addition of anti-adherents as excipients. The tablets formed has a friability of less than 1% and a crushing strength of 5Kgf, as seen in Table 5. The release kinetics and mechanism of the drug is seen in Table 6 and Figure 2. It shows that the tablets using *Sida acuta* gum released more than 95% of the drug over the 8 hour period of the study, and followed a zero order release kinetics.

Table 4: Micromeritics and Flow Properties of Granules

Batch/ parameter	Bulk density (g/ml)	Tapped density (g/ml)	Flow rate (g/s)	Carr's index (%)	Hausner's ratio	Angle of repose (°)	Granule porosity (%)	True density (g/ml)
G1	0.31±0.00	0.35±0.01	5.19±0.00	11.43±0.02	1.13±0.01	33.69	74.60±0.38	1.22±0.00
G2	0.30±0.01	0.34±0.00	5.60±0.00	11.76±0.01	1.13±0.01	31.29	75.61±0.02	1.23±0.00

Key: G1= Granules containing guar gum

G2 = Granules containing *Sida acuta* gum

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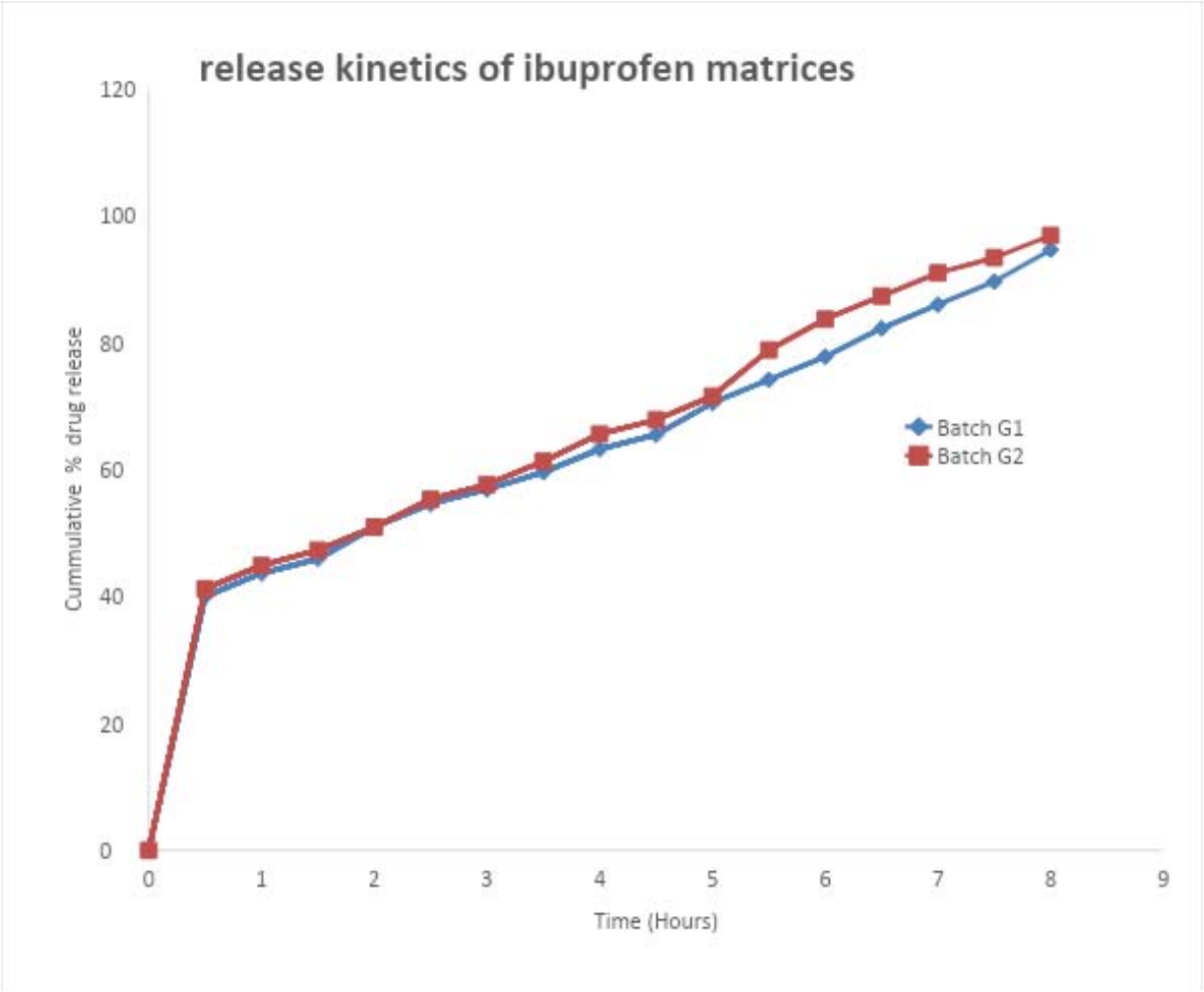
Table 5: Physical Properties of Ibuprofen Sustained Release Tablet

Batch /Parameters	Weight uniformity (g)	Hardness (Kgf)	Diameter (mm)	Thickness (mm)	Friability (%)	Content uniformity (%)
G1	0.40±0.02	5.00±0.01	12.61±0.00	3.26±0.01	0.99±0.00	105±1.00
G2	0.41±0.02	5.05±0.01	12.61±0.01	3.27±0.01	0.84±0.01	103±2.00

Key: G1 Ibuprofen tablets containing guar gum
G2 Ibuprofen tablets containing *Sida acuta* gum

Table 6: Release Kinetics of Ibuprofen Tablets

Batches	Zero Order (R^2)	First Order (R^2)	Higuchi (R^2)	Korsemeyer/Peppas (R^2)	n(diffusion coefficient)	t_{50} h
G1	0.9961	0.8739	0.9582	0.9225	0.0230	1.90
G2	0.9661	0.8692	0.953	0.9117	0.0110	1.90



Key: G1 is tablet matrix with guar gum
G2 is tablet matrix with *Sida acuta* gum

Fig. 2: Release profile of Ibuprofen matrices using natural gums

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IV. Discussion

The yield of the *Sida acuta* gum from the leaves of the plant is very low as compared to other gums from seeds or exudates from the stem [4, 8]. The result seen from the Ruthenium and Molisch tests for the *Sida acuta* gum is same for guar, indicating confirmation of the obtained gum. The pH of natural polymers is a useful parameter in determining their suitability for pharmaceutical formulations. This is because the solubility and stability of active ingredients are a function of the pH which can be influenced by an excipient's pH. *Sida acuta* being 5.88 in pH is weakly acidic (Table 2) while that may make the gum not suitable for use in drug formulations that might stay longer in the buccal cavity because of a possible mucosa irritation. It can, however, be useful as uncoated tablet matrix without gastric irritation [9].

a) Swelling index and Hydration capacity

The swelling index of the *Sida acuta* gum is relatively high with a value of 8.36% although lesser than that of guar gum. The degree of swelling of a gum reveals its capacity of its individual particles to absorb water molecules and increase in size on hydration. The swelling index value of natural gums together with their simplicity and cheap production process has been reported to be reasons for their suitability for use as release modifying polymers, one way guar gum is used [10,11]. For the flow properties, Guar gum has been reported to have a good flow[12]. There is no statistical difference between the flow of the granules of both gums when tested at $p \leq 0.05$. It means that granules formed from both gums can be directly compressed without anti-adherents as excipients.

b) Mechanical properties of Tablets

The mechanical properties of the tablets show no statistically significant difference (at $p \leq 0.05$) for both gums in the crushing strength, friability, and tensile strength, hence on the basis of obtaining tablets with satisfactory friability and crushing strength, any of the gum could be used interchangeably. However a more sensitive parameter to determine the mechanical strength of tablets, the crushing strength friability ratio (CSFR), reveals that tablets with *Sida acuta* gum as matrix-former were mechanically stronger (CSFR value of 6.01) than those of guar gum (CSFR is at 5.05).

c) Dissolution studies and Release kinetics

The release kinetics of the drug is seen in Figure 2. It shows that both gums sustained the release of the drug over a period of 8 hours giving a cumulative percentage of release to be almost 100% (specifically 96% for *Sida acuta* but 94% for Guar). At the 6h, 77% and 83% of drug was released from tablet batches of G1 and G2 respectively. Similar release kinetics was reported by Jaleh *et al.,* (2006) for natural gums such as guar gum [12]. Thus, both gums qualify as excipients for sustained release. Drug release from a tablet matrix involves concurrent penetration of matrix by the surrounding dissolution medium, drug dissolution and drug leak out through the interstitial channels within the matrix. The interplay of these three processes predicts the drug release kinetics and is usually influenced by the physicochemical properties of the drug and the polymer[13,14]. It is worthy to note that while t_{50} (that is the time for 50% of the drug release) for batches of tablets of both gums was the same (1.9 h), after 5 h, batch of tablet with *Sida acuta* released higher percentage of the active ingredient and maintained it until the 8th h when it returned to the rate of release of the tablet with guar gum. This observation may be explained with the inter particulate arrangement of the gum when well hydrated in an aqueous medium. The higher swelling index value of guar gum whose gel mass retarded the drug release in the matrix core from the 5th h, may likely be responsible. A similar value for t_{50} was reported by Eziuzo *et al.,* (2017)[15] in his kinetic studies of diclofenac matrix tablet using *Sida acuta.*

The data from the dissolution studies of the two batches of drug were subjected to four drug release models and correlation coefficient (the linearity of R^2 values) describes the likely release model. The two batches of tablets released their drug content following the zero order (Table 6). This means the same concentration of the drug is released with time throughout the period of the study irrespective of the amount of the drug that is left in the matrix. Thus, drug release process is constant and independent of initial concentration of drug in the drug delivery matrix [13]. Sustained release matrix tablets of *Sida acuta* and other solid dosage forms using natural gums or their blends have been reported to follow this course of drug release although a controlled release could have different concentration released at different times as intended.[10,12,13, 15]

V. Conclusion

Sida acuta gum modified the release of ibuprofen over a sustained period of 8 h, had good swelling index and favorable micromeritics that can make it qualify for polymer useful in sustained release even as a directly compressible excipient. It is equally valuable in use as a substitute for guar gum although the main challenge is in the yield. This no doubt requires further work to see how it can be improved.

a) Significant statement

This study, therefore, discovers the release modifying potential of *Sida acuta* hydrocolloid comparing favorably well with guar gum, a bio-polymer that can be beneficial for application in sustained release formulations. This study will help the researcher to uncover another source for tablet matrix-former from

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Sida acuta leaves that many researchers were yet to explore. However, with the low yield got, a new process on improving yield of the hydrocolloid may be investigated.

Conflict of Interest: None

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Association between Quality of Sleep and its Effect on Glycaemic Control in Patients with Type 2 Diabetes Mellitus- A Pilot Study

By Dr. Firas Rauf Mammoo & Prof. Dr. S. Girija

Introduction- Diabetes mellitus is a common metabolic disease. Nowadays, sleep complaints are increasing day by day due to the restriction in bed time resulting in chronic partial sleep loss.(1) Type 2 diabetes mellitus accounts for 95% of all of diagnosed diabetes worldwide. Several studies have recognized sleep disorder as a novel risk factor for diabetes.(2) Sleep disorder plays a vital role in the development of diabetes via various metabolic and neuroendocrine pathways.(3) Nocturia and neuropathic pain were explained as two possible causes of decreased sleep quality.(1) People who have sleep disorder either in the quality or quantity experienced reduced insulin sensitivity, which results in elevated blood glucose that can aggravate the progress of diabetes. There are limited studies from India on the association of sleep quality and diabetes control status. In this study, we aimed to find the quality of sleep in patients with type 2 diabetes mellitus and its correlation with glycaemic control.

GJMR-B Classification: NLMC Code: WK 810



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Association between Quality of Sleep and its Effect on Glycaemic Control in Patients with Type 2 Diabetes Mellitus- A Pilot Study

Dr. Firas Rauf Mammoo [α] & Prof. Dr. S. Girija [σ]

I. Introduction

Diabetes mellitus is a common metabolic disease. Nowadays, sleep complaints are increasing day by day due to the restriction in bed time resulting in chronic partial sleep loss.[1] Type 2 diabetes mellitus accounts for 95% of all of diagnosed diabetes worldwide. Several studies have recognized sleep disorder as a novel risk factor for diabetes.[2] Sleep disorder plays a vital role in the development of diabetes via various metabolic and neuroendocrine pathways.[3] Nocturia and neuropathic pain were explained as two possible causes of decreased sleep quality.[1] People who have sleep disorder either in the quality or quantity experienced reduced insulin sensitivity, which results in elevated blood glucose that can aggravate the progress of diabetes. There are limited studies from India on the association of sleep quality and diabetes control status. In this study, we aimed to find the quality of sleep in patients with type 2 diabetes mellitus and its correlation with glycaemic control.

II. Material and Methods

It is a hospital record-based descriptive and cross-sectional analytical study involving patients with type 2 diabetes mellitus. The patients for the study were recruited from the outpatients and inpatients attending the Department of General Medicine of Sri Manakula Medical College and Hospital for a period six months after obtaining ethical committee approval.

Sample size: The sample size was determined by a single population- proportion formula with the assumptions of the 95% confidence level, 7.5% precision. The sample size was calculated for variables such as poor sleep quality, which is 33.8 %, and considering a 10% non-responses rate; the sample size was further increased to 160 respondents.[1]

Patients over 18 years old with a duration of diabetes more than one year were recruited for the study.

Patients with type 1 diabetes, gestational diabetes, or other specific types of diabetes, patients with acute diabetic complications, severe heart diseases, lung diseases, and cerebral diseases, patients with mental illness, and those with intelligence or cognitive impairment was excluded from the study.

Data collection procedure: Necessary data were collected in two stages. The details like demographic, risk factors, diabetic control, biochemical indicators HbA1c, complication, etc. were extracted in the questionnaire from the OPD and IP registration card. The patients fulfilling the inclusion criteria were recruited for the study after obtaining informed consent. Quality of sleep was measured using pittsburgh quality of sleep index, which measures seven components, which included subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction over the last one month.

Data analysis: As a first step, the frequency tables were obtained for discrete variables such as socio-demographic characteristics, risk factors, diabetic status, biochemical indicators, HbA1c, waist-hip ratio, and body mass index, and complications. Continuous variables were expressed as mean and standard deviation. Chi-square (x2) test was applied to proportions to find the level of significance which is fixed at $p<0.05$. Confidence interval (CI) set at 95%. Ethical principles such as respect for the persons, beneficence, justice, and ensuring confidentiality and privacy adhered to throughout the study. Ethical clearances was obtained from the institutional ethical committee.

III. Results

A total of 160 patients with type 2 diabetes mellitus were recruited for the study. The sociodemographic and clinical characteristics of the patients are shown in Table.1. The mean (SD) age of the patients was 55.5 (12.1%) years. One-fourth of patients had Diabetes Mellitus for more than five years. Almost three-fourth (117 patients) had uncontrolled PPBS, and three- fifths (94 patients) had uncontrolled FBS; in total, 79.4% (n=127) had an uncontrolled type 2 diabetes mellitus status. The proportion of patients with HbA1c > 6.1 was 91.9%. Quality of sleep was deficient in 18.1% (95% CI 12.5-24.9) (Figure.1). Around two-fifths (n=61, 38%) reported hypertension as co-morbidity.

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The correlation between PSQI with the duration of type 2 diabetes mellitus, FBS, PPBS and HbA1c are depicted in Table 2. There was a moderately positive correlation between PSQI score and PPBS (r=0.53) and low positive correlation for FBS (r=0.33) and HbA1c (r=0.49).

The association of age, gender, duration of diabetes, fasting, postprandial blood glucose, and Hba1c on sleep quality are shown in Table 3 and Table 4. Compared to a younger age group, diabetic patients aged 51-60 years had a higher risk of poor glycaemic control (aPR=1.34). Males had uncontrolled diabetes compared to females but were not found to be statistically significant (aPR=1.01, p=0.91). Having hypertension with type 2 diabetes mellitus had 1.16 times higher risk for poor glycaemic control. Type 2 diabetes mellitus duration for more than five years increases the chance of uncontrolled DM (aPR=1.21, p=0.02).

IV. Discussion

Short term studies have shown that disturbed or reduced sleep is associated with glucose intolerance and insulin resistance, thus predisposing the individual to type 2 diabetes mellitus. One potential mechanism includes reciprocal changes in circulating levels of leptin and ghrelin, which in turn increases appetite and obesity.[6] Sleep deprivation is said to decrease insulin production by increasing cortisol levels. Patients with diabetes tend to have many intrinsic and extrinsic sleep disorders.

This study was done to assess the quality of sleep and its relation with glycaemic control among type 2 diabetes mellitus patients using PSQI and the results showed that 18% of our study patients were having poor sleep (PSQI > 5), which is less than what other studies showed.[1] The mean (SD) of total PSQI score was 3.75 (2.7%), and this was similar to a study done in the USA by Luyster and Dunbar-Jacob.[7] But it was lower than other studies which reported a higher mean score of PSQI.[3-5] A meta-analysis conducted in 2010 reported poor sleep quality as a known risk factor for T2DM.[6] A study showed that a reduction of sleep by 2 hours for one week in young, healthy men and women were associated with a significant increase in the secretion of pro-inflammatory cytokines IL6 and TNF α which can lead to increased insulin resistance and cardiovascular disease.[8]

The current study showed a moderate positive correlation between PSQI score and HbA1c. Patients with high HbA1c levels tend to have increased symptoms such as thirst, nocturia, and neuropathic pain, which could lead to short sleep duration and poor sleep quality.[7] Similarly, poor sleep quality leads to elevation of the levels of cortisol, IL-6, and TNFα, resulting in activation of the sympathetic nervous system that promotes insulin resistance.[8, 9] Reduction in sleep duration may interfere the daytime activities and may prevent the patient from adherence to medications, diet and exercises. There is a need for more studies to understand the mechanisms underlying.

The present study indicated that 79% of the patient's glycaemic status were not under control (FBS>125mg/dl or PPBS>200mg/dl). These findings are similar to a large pan-India cross- sectional registry study conducted by Borgharkar et al. between 2015 and 2017.[10] Our results showed that only age, duration of diabetes, and poor sleep quality are the independent predictors of uncontrolled T2DM. These findings were in agreement with the results of some studies.[1, 11] Younger patients with diabetes mellitus (<50 years) were found to be associated with poor glycaemic control due to high insulin resistance.[14]

Our study found that duration of diabetes is one of the determinants of poor glycaemic control. A study conducted by Herrington et al. also identified the effect of long duration on poor glycemic control.[12] Deficient sleep quality is associated with a higher number of co-morbidities, higher number of diabetic complications and depression as reported by Luyster in his study.[7]

The limitations of this study could be that the majority of the study population were men (62%), and gender variations of sleep and diabetes are not adequately addressed. Only selective patients were questioned which may give results that might not be representative of the entire population with diabetes. Finally, no information on psychological parameters, type of medications, medication adherence, and comorbidities other than hypertension that might affect diabetes control was collected. No objective validation of sleep by means of polysomnography, EEG or EMG were done.

V. Conclusion

It is imperative to assess sleep in all patients with diabetes mellitus, and if needed a complete sleep study may be recommended. If identified, strategies to improve sleep quality and psychological consultation should be provided.

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Table 1: Sociodemographic and clinical details (N=160)

Variable	n	%
Age in years		
Up to 50	55	34.4
51-60	48	30.0
60 above	57	35.6
Gender		
Male	100	62.5
Female	60	37.5
Hypertension		
Yes	61	38.1
No	99	61.9
Diabetes duration		
Upto 5 years	119	74.4
More than 5 years	41	25.6
FBS control status		
Controlled	66	41.3
Uncontrolled	94	58.8
PPBS control status		
Controlled	43	26.9
Uncontrolled	117	73.1

Table 2: Correlation between PSQI with DM duration, FBS, PPBS, HBA1C (N=160)

Variable	Correlation coefficient
DM duration	0.141
FBS	0.327
PPBS	0.533
Hba1c	0.493

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Table 3: Association of sleep, Sociodemographic and clinical factors with FBS and PPBS (N=160)

Variable	T2DM		Crude PR	Adjusted PR	P value
	Uncontrolled (FBS>126/PPBS>183)	Controlled (FBS≤126/PPBS≤183)			
Age in year					
Up to 50 Years	48 (87.3)	7 (12.7)	1.26	1.34	0.01
51-60	33 (68.8)	15 (31.3)	1	1	-
60 above	46 (80.7)	11 (19.3)	1.17	1.14	0.252
Gender					
Male	80 (80.0)	20 (20.0)	1.02	1.01	0.91
Female	47 (78.3)	13 (21.7)	1	1	-
DM duration					
Up to 5 years	90 (75.6)	29 (24.4)	1	1	0.02
More than 5 years	37 (90.2)	4 (9.7)	1.19	1.21	-
Hypertension					
Yes	53 (86.9)	8 (13.1)	1.16	1.08	0.321
No	74 (74.7)	25 (25.3)	1	1	-
Sleep Quality					
Poor	27 (93.1)	2 (6.9)	1.22	1.17	0.022
Good	100 (76.3)	31 (23.7)	1	1	-

Table 4: Association of sleep, sociodemographic and clinical factors with HbA1c (N=160)

Variable	T2DM		Crude PR	Adjusted PR	P value
	Uncontrolled (Hba1c>6.1)	Controlled (Hba1c≤6.1)			
Age in year					
Up to 50 Years	53 (96.4)	2 (3.6)	1.08	1.14	0.039
51-60	43 (89.6)	5 (10.4)	1.01	1.02	0.290
60 above	51 (89.5)	6 (10.5)	1	1	-
Gender					
Male	93 (93.0)	7 (7.0)	1.03	1.02	0.697
Female	54 (90.0)	6 (10.0)	1	1	-
DM duration					
Up to 5 years	106 (89.1)	13 (10.9)	1	1	0.001
More than 5 years	41 (100.0)	0 (0)	1	1.14	-
Hypertension					
Yes	59 (96.7)	2 (3.3)	1.09	1.05	0.200
No	88 (88.9)	11 (11.1)	1	1	-
Sleep Quality					
Poor	29 (100)	0 (0)	1	1.08	0.014
Good	118 (90.1)	13 (9.9)	1	1	-

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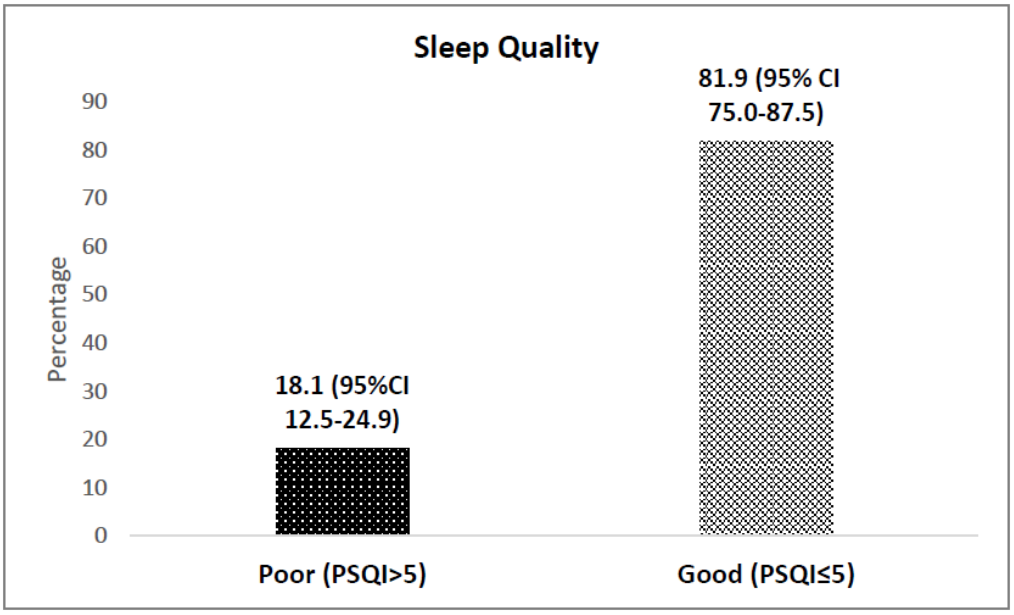


Figure 1: Prevalence of poor sleep among Type 2 Diabetes Mellitus patients

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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.



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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.



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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.



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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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