GOKULA KRISHNA COLLEGE OF PHARMACY

HEI CODE: C-26844	NAAC SSR	CYCLE I

3 : RESEARCH, INNOVATIONS & EXTENSION

3.3 Research Publications and Awards	3.3.1 No. of Research Papers Published per Teacher during the last five years

3.3.1 Research Papers Published during the last five years

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LIST OF PATENTS GRANTED / PUBLISHED IN THE LAST FIVE YEARS

S.No	Name of the Inventor (s)	Application No	Title of the Patent	Status	Agency to which application is made	Date
1	Dr Balagani Pavan Kumar	383386-001	Portable Electro Spinning Device for Development of Nanofibres	Applied	Intellectual Property India	08-04-2023
2	Dr Balagani Pavan Kumar	2021104266	Enhanced Effectiveness of Meloxicam Through Hydrogel Formulations	Granted	Commissioner of Patents, Australia	25-08-2021
3	Dr Balagani Pavan Kumar	2021104955	Reversible Hydrogel Formulation for Prolonged Antimicrobial Activity	Granted	Commissioner of Patents, Australia	02-11-2021

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Design Application Details

Application Number:

383386-001

Cbr Number:

204430

Cbr Date:

08/04/2023 22:02:29

Applicant Name:

1. Dr. Sachinkumar Dnyaneshwar Gunjal **2. Dr. Balagani Pavan Kumar** **3. Dr. Channabasavaraj. S**
4. Bhawana Kapoor **5. Mr. Vishal ramdas tagalpallewar** **6. Dr. B.Sree Giri Prasad**
7. Dr.Navakanth Raju Ramayanam **8. Dr. Satyanarayan Pattnaik**

Design Application Status

Application Status:

Examination Report has been Generated ,Online Reply Document Recived(FER generated on 19/06/2023)

Back (/DesignApplicationStatus/)

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Australian Government

IP Australia

CERTIFICATE OF GRANT

INNOVATION PATENT

Patent number: 2021104955

The Commissioner of Patents has granted the above patent on 2 November 2021, and certifies that the belowparticulars have been registered in the Register of Patents.

Name and address of patentee(s):

Dr.Balagani Pavan Kumar, Gokula Krishna College of Pharmacy,Sullurpet,SPSR Nellore,Andhra Pradesh, India - 524121

Dr. G. Sridhar Babu, Sri Shivani College of Pharmacy,Doctor's colony,near mulugu road,Warangal, India - 506007

Dr Bhavani Boddeda, Koringa College of Pharmacy,Korangi,East Godavari,Andhra Pradesh, India

Dr. Manish Kumar Thimmaraju, Balaji Institute of Pharmaceutical Sciences,Narsampet,Warangal,Telangana, India - 506132

Dr.Goje Arjun, Teegala Ram Reddy College of Pharmacy,Hyderabad, Telangana, India

Title of invention:

REVERSIBLE HYDROGEL FORMULATION FOR PROLONGED ANTIMICROBIAL ACTIVITY

Name of inventor(s):

Kumar, Balagani Pavan ; Babu, G. Sridhar ; Boddeda, Bhavani ; Thimmaraju, Manish Kumar ; Arjun, Goje

Term of Patent:

Eight years from 5 August 2021

NOTE: This Innovation Patent cannot be enforced unless and until it has been examined by the Commissioner of Patents and a Certificate of Examination has been issued. See sections 120(1A) and 129A of the Patents Act 1990, set out on the reverse of this document.

Dated this 2nd day of November 2021

Commissioner of Patents

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PATENTS ACT 1990

Australian Government

IP Australia

CERTIFICATE OF GRANT

INNOVATION PATENT

Patent number: 2021104266

The Commissioner of Patents has granted the above patent on 25 August 2021, and certifies that the below particulars have been registered in the Register of Patents.

Name and address of patentee(s):

Manish Kumar Thimmaraju of Balaji Institute of Pharmaceutical Sciences, Narsampet Warangal Telangana 506132 India

G Sridhar Babu of Sri Shivani College of Pharmacy, Doctor's colony. Near Mulugu road Warangal Telangana 506007 India

Balagani Pavan Kumar of Gokula Krishna College of Pharmacy, Sullurpet SPSR Nellore Andhra Pradesh 524121 India

Deepak Kumar of Ranchi College of Pharmacy, Kute ToliTetri, Namkum Ranchi Jharkhand 834010 India

Goje Arjun of Teegala Ram Reddy College of Pharmacy Hyderabad Telangana India

Title of invention:

ENHANCED EFFECTIVENESS OF MELOXICAM THROUGH HYDROGEL FORMULATIONS

Name of inventor(s):

Thimmaraju, Manish Kumar; Babu, G. Sridhar; Kumar, Balagani Pavan; Kumar, Deepak and Arjun, Goje

Term of Patent:

Eight years from 17 July 2021

NOTE: This Innovation Patent cannot be enforced unless and until it has been examined by the Commissioner of Patents and a Certificate of Examination has been issued. See sections 120(1A) and 129A of the Patents Act 1990, set out on the reverse of this document.

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Dated this 25th day of August 2021

Commissioner of Patents

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NO. OF RESEARCH PAPERS PUBLISHED PER TEACHER IN THE JOURNALS NOTIFIED ON UGC CARE LIST DURING THE LAST FIVE YEARS

CALENDER YEAR - 2022

S.No	Title of the Paper	Name of the Author/s	Name of the Journal	ISSN No
1	Development and validation of an HPLC-UV method for analysis of methylphenidate hydrochloride and loxapine succinate in an activated carbon disposal system	Mrs B Swathi	International Journal of Gender, Science and Technology	2040-0748
2	Development and validation of an HPLC-UV method for analysis of methylphenidate hydrochloride and loxapine succinate in an activated carbon disposal system	Mrs P Kavitha	International Journal of Gender, Science and Technology	2040-0748
3	Development and validation of an HPLC-UV method for analysis of methylphenidate hydrochloride and loxapine succinate in an activated carbon disposal system	Mrs CH Harika	International Journal of Gender, Science and Technology	2040-0748
4	Development and validation of an HPLC-UV method for analysis of methylphenidate hydrochloride and loxapine succinate in an activated carbon disposal system	Mr Y Naveen Kumar	International Journal of Gender, Science and Technology	2040-0748
5	Development and validation of an HPLC-UV method for analysis of methylphenidate hydrochloride and loxapine succinate in an activated carbon disposal system	Mr.AVLS Ramakrishna	International Journal of Gender, Science and Technology,	2040-0748
6	Magnetic-silk/polyethyleneimine core-shell nanoparticles for targeted gene delivery into human breast cancer cells	Dr.Balagani Pavan Kumar	Indo-American Journal of Pharma and Bio science	2347-2251

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7	Magnetic-silk/polyethyleneimine core-shell nanoparticles for targeted gene delivery into human breast cancer	Mr.M.Kalyan babu	Indo-American Journal of Pharma and Bio science	2347-2251
8	Magnetic-silk/polyethyleneimine core-shell nanoparticles for targeted gene delivery into human breast cancer	Mr.N.Praveenkumar	Indo-American Journal of Pharma and Bio science	2347-2251
9	A Study on Synthesis and Characterization of some Novel Quinazolinones.	P.Sivakumar	European Journal of Biomedical and Pharmaceutical Sciences	2349-8870
10	Pharmacokinetic Variability in Pediatrics and Intensive care / towards a personalized dosing approach	Mrs D Kalyani	Indo-American Journal of pharma and Bio science	2347-2251
11	Pharmacokinetic Variability in Pediatrics and Intensive care / towards a personalized dosing approach	Ms A R Sridevi	Indo-American Journal of pharma and Bio science	2347-2251
12	Pharmacokinetic Variability in Pediatrics and Intensive care / towards a personalized dosing approach	Mrs P Sukanya	Indo-American Journal of pharma and Bio science	2347-2251
13	Pharmacokinetic Variability in Pediatrics and Intensive care / towards a personalized dosing approach	Mrs A Aksa anvija	Indo-American Journal of pharma and Bio science	2347-2251
14	Pharmacokinetic Variability in Pediatrics and Intensive care / towards a personalized dosing approach	Mr C G Bhaskar	Indo-American Journal of pharma and Bio science	2347-2251
15	How Solvents Affect the Rate of Polymorphic Transformation in Polymorph Screening	Mrs D Kalyani	History of Medicine studies	1300-669

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16	How Solvents Affect the Rate of Polymorphic Transformation in Polymorph Screening	Mrs T Swathi	History of Medicine studies	1300-669
17	How Solvents Affect the Rate of Polymorphic Transformation in Polymorph Screening	Mrs P Sukanya	History of Medicine studies	1300-669
18	How Solvents Affect the Rate of Polymorphic Transformation in Polymorph Screening	Mrs CH Harika	History of Medicine studies	1300-669
19	How Solvents Affect the Rate of Polymorphic Transformation in Polymorph Screening	Mrs K Vanitha Devi	History of Medicine studies	1300-669
20	The Sensitive Method of Subvisible Particle Counting for the Detection and Quantification of Monoclonal Antibody Aggregation Caused by Freeze-Thawing: New Understanding of Particle Function in the Protein Aggregation Process	Mrs N Sukanya	History of Medicine studies	1300-669
21	The Sensitive Method of Subvisible Particle Counting for the Detection and Quantification of Monoclonal Antibody Aggregation Caused by Freeze-Thawing: New Understanding of Particle Function in the Protein Aggregation Process	Mrs P K Devibala	History of Medicine studies	1300-669
22	The Sensitive Method of Subvisible Particle Counting for the Detection and Quantification of Monoclonal Antibody Aggregation Caused by Freeze-Thawing: New Understanding of Particle Function in the Protein Aggregation Process	Ms.SK Zoofishaan	History of Medicine studies	1300-669

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23	The Sensitive Method of Subvisible Particle Counting for the Detection and Quantification of Monoclonal Antibody Aggregation Caused by Freeze-Thawing: New Understanding of Particle Function in the Protein Aggregation Process	Mr.M R Pavan Kumar	History of Medicine studies	1300-669
24	The Sensitive Method of Subvisible Particle Counting for the Detection and Quantification of Monoclonal Antibody Aggregation Caused by Freeze-Thawing: New Understanding of Particle Function in the Protein Aggregation Process	Mr S Sivakoteswa Rao	History of Medicine studies	1300-669
25	Cytotoxic Compounds from Kibataliagitingensis (Elm.) Woodson	Dr.P Kishor	International Journal of Gender, Science and Technology	2040-0748
26	Cytotoxic Compounds from Kibataliagitingensis (Elm.) Woodson	Mr.Sivakumar Peta	International Journal of Gender, Science and Technology	2040-0748
27	Cytotoxic Compounds from Kibataliagitingensis (Elm.) Woodson	Dr.M Soujanya	International Journal of Gender, Science and Technology	2040-0748
28	Cytotoxic Compounds from Kibataliagitingensis (Elm.) Woodson	Mrs S Usha Rani	International Journal of Gender, Science and Technology	2040-0748
29	Cytotoxic Compounds from Kibataliagitingensis (Elm.) Woodson	Mrs Vanitha Devi	International Journal of Gender, Science and Technology	2040-0748
30	Development and Standardization of a Polyherbal Anti-Urolithiatic Suspension	Pallepati Kishor	Future Journal of Pharmaceutical and Health Sciences	2583-116X

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31	Development and Standardization of a Polyherbal Anti-Urolithiatic Suspension	Pallepati Kavitha	Future Journal of Pharmaceutical and Health Sciences	2583-116X
32	Development and Standardization of a Polyherbal Anti-Urolithiatic Suspension	Sivakumar Peta	Future Journal of Pharmaceutical and Health Sciences	2583-116X

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Development and validation of an HPLC-UV method for analysis of methylphenidate hydrochloride and loxapine succinate in an activated carbon disposal system

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A B S T R A C T

Unauthorized persons run the risk of abusing unused pharmaceuticals, which may lead to significant injury. In order to keep people safe and keep the environment free of any dangers, the Food and Drug Administration (FDA) recommends that people properly dispose of any unwanted prescription medicine. Unfortunately, safety is an issue that is overlooked by many of the present disposal methods. Granular activated carbon, when added to a drug disposal pouch, provides a novel, easy, and safe way to dispose of unused or expired medicine. We examined the disposal system's deactivation effectiveness and developed a robust and verified technique for methylphenidate hydrochloride and loxapine succinate using high-performance liquid chromatography (HPLC). A C18 analytical column with the following dimensions: 250 mm × 4.60 mm and 100Å, was used to evaluate methylphenidate hydrochloride. The mobile phase consisted of acetonitrile-water with 0.05% (v/v) trifluoroacetic acid, and the flow rate was

1.5 mL/min, with a 15-minute run and a 7.8-minute retention period. Using a flow rate of 1.0 mL/min, loxapine succinate was isolated on a C8 100Å column (250 mm × 4.6 mm, 5 mm) that was kept at 25 °C. The medication had a retention duration of around 4.6 minutes, and the run time was 10 minutes. At a pH of 3.0, the mobile phase consisted of 40:60 (v/v) acetonitrile and water with 0.3% triethylamine. Both medications were dissolved in mobile phases to create reference standard solutions with a concentration of 100 mg/mL. Over the concentration range of 5-100 mg/mL for methylphenidate hydrochloride and 0.1-100 mg/mL for loxapine succinate, these techniques exhibit acceptable linearity (R2 ¼ 0.999). Research on the inactivation of these medications made good use of the test methodologies. Xi'an Jiaotong University, 2018. This website is created and hosted by Elsevier B.V. An open access paper published in accordance with the

1. Introduction

A major issue now is how to properly dispose of leftover prescription drugs. Accidental exposure, purposeful use or misuse, or both might result from storing undesired or outdated pharmaceuticals. There are social and economic ramifications to the public health problem of th possibility of abuse and addiction to prescriptic pharmaceuticals, even those used to treat pain. Hero addiction affected 591,000 people in 2015, and ov 33,000 people died from opioid overdoses or drug misu disorders associated with prescription opioid painkille [1,2]. Medication is a lifesaver when it comes to alleviatir acute and severe chronic pain, but it may have disastrou consequences when prescribed excessively or witho proper safety measures. The National Survey on Dru usage and Health found that after five years of non-medic prescription painkiller usage, less than 4% of individua began using heroin [1]. Therefore, it is important t dispose of prescription medicine correctly. The disposal two psychoactive drugs, loxapine succinate an methylphenidate hydrochloride (MPH), was the primar focus of the current investigation.By activating th neurological system, the popular prescription medicin MPH influences the brain's dopamine balance, making it a effective treatment for attention-deficit hyperactivit disorder (ADHD) [3]. When administered intranasall MPH has a pharmacological effect comparable to cocain resulting in a fast release of dopamine [4]. Like morphin it has the potential to create serious physiologic dependency and is hence classified as a Schedule I federally-controlled narcotic, due to its significant abus potential. Because of its very satisfying euphoric effect MPH is highly addictive [5]. Lozapine succinate is anothe medicine with abuse potential. For schizophrenia, doctor prescribe this medicine, which is a tricyclic antipsychoti To control the thoughts, feelings, and behaviors ofte associated with schizophrenia, loxapine succinate i administered by inhibiting the activity of dopamine. Th misuse of loxapine succinate is possible since it is used for the management of schizophrenia an only gives short relief [6]. There is a higher risk of misus for these medicines because of how often they are given.

Given the considerable misuse potential of MPH and loxapine succinate, we aimed to explore their deactivation profile via the drug disposal system. Also investigated was the analytical accuracy of the developed technique for both medications. There aren't many analytical procedures for loxapine succinate [9] and MPH [7,8] published in the

Development and validation of an HPLC-UV method for analysis of methylphenidate hydrochloride and loxapine succinate in an activated carbon disposal system

Mrs B Swathi ,Mrs P Kavitha,Mrs CH Harika,Mr Y Naveen Kumar ,Mr.AVLS Ramakrishna
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A B S T R A C T

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Development and validation of an HPLC-UV method for analysis of methylphenidate hydrochloride and loxapine succinate in an activated carbon disposal system

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A B S T R A C T

Unauthorized persons run the risk of abusing unused pharmaceuticals, which may lead to significant injury. In order to keep people safe and keep the environment free of any dangers, the Food and Drug Administration (FDA) recommends that people properly dispose of any unwanted prescription medicine. Unfortunately, safety is an issue that is overlooked by many of the present disposal methods. Granular activated carbon, when added to a drug disposal pouch, provides a novel, easy, and safe way to dispose of unused or expired medicine. We examined the disposal system's deactivation effectiveness and developed a robust and verified technique for methylphenidate hydrochloride and loxapine succinate using high-performance liquid chromatography (HPLC). A C18 analytical column with the following dimensions: 250 mm × 4.60 mm and 100Å, was used to evaluate methylphenidate hydrochloride. The mobile phase consisted of acetonitrile-water with 0.05% (v/v) trifluoroacetic acid, and the flow rate was

1.5 mL/min, with a 15-minute run and a 7.8-minute retention period. Using a flow rate of 1.0 mL/min, loxapine succinate was isolated on a C8 100Å column (250 mm × 4.6 mm, 5 mm) that was kept at 25 °C. The medication had a retention duration of around 4.6 minutes, and the run time was 10 minutes. At a pH of 3.0, the mobile phase consisted of 40:60 (v/v) acetonitrile and water with 0.3% triethylamine. Both medications were dissolved in mobile phases to create reference standard solutions with a concentration of 100 mg/mL. Over the concentration range of 5-100 mg/mL for methylphenidate hydrochloride and 0.1-100 mg/mL for loxapine succinate, these techniques exhibit acceptable linearity (R2 ¼ 0.999). Research on the inactivation of these medications made good use of the test methodologies. Xi'an Jiaotong University, 2018. This website is created and hosted by Elsevier B.V. An open access paper published in accordance with the

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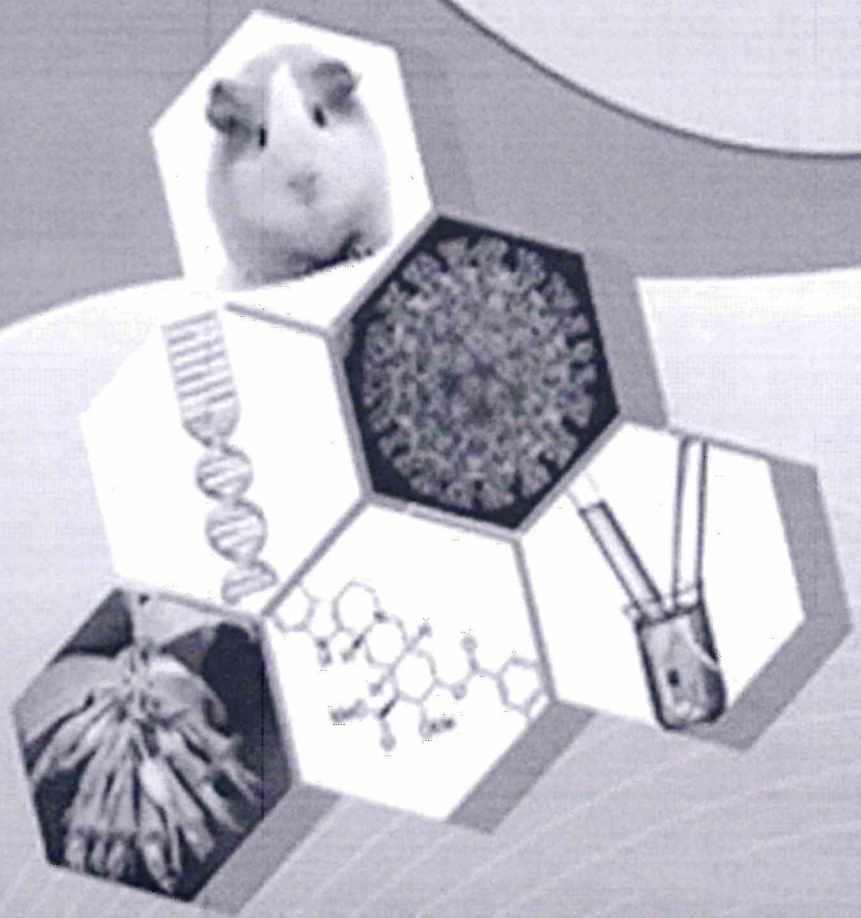

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Magnetic-silk/polyethyleneimine core-shell nanoparticles for targeted gene delivery into human breast cancer cells

Dr.Balagani Pavan Kumar , Mr.M.Kalyan babu , Mr.N.Praveenkumar

A B S T R A C T

The lack of efficient and cost-effective methods for gene delivery has significantly hindered the applications of gene therapy. In this paper, a simple one step and cost effective salting-out method has been explored to fab- ricate silk-PEI nanoparticles (SPPs) and magnetic-silk/PEI core-shell nanoparticles (MSPPs) for targeted delivery of c-myc antisense oligodeoxynucleotides (ODNs) into MDA-MB-231 breast cancer cells. The size and zeta po- tential of the particles were controlled by adjusting the amount of silk fibroin in particle synthesis. Lower surface charges and reduced cytotoxicity were achieved for MSPPs compared with PEI coated magnetic nanoparticles (MPPs). Both SPPs and MSPPs were capable of delivering the ODNs into MDA-MB-231 cells and significantly inhibited the cell growth. Through magnetofection, high ODN uptake efficiencies (over 70%) were achieved within 20 min using MSPPs as carriers, exhibiting a significantly enhanced uptake effect compared to the same carriers via non-magnetofection. Both SPPs and MSPPs exhibited a significantly higher inhibition effect against MDA-MB-231 breast cancer cells compared to human dermal fibroblast (HDF) cells. Targeted ODN delivery was achieved using MSPPs with the help of a magnet, making them promising candidates for targeted gene therapy applications.

Keywords: Silk PEIMagnetic nanoparticles Gene deliveryCancer ODN Magnetofection

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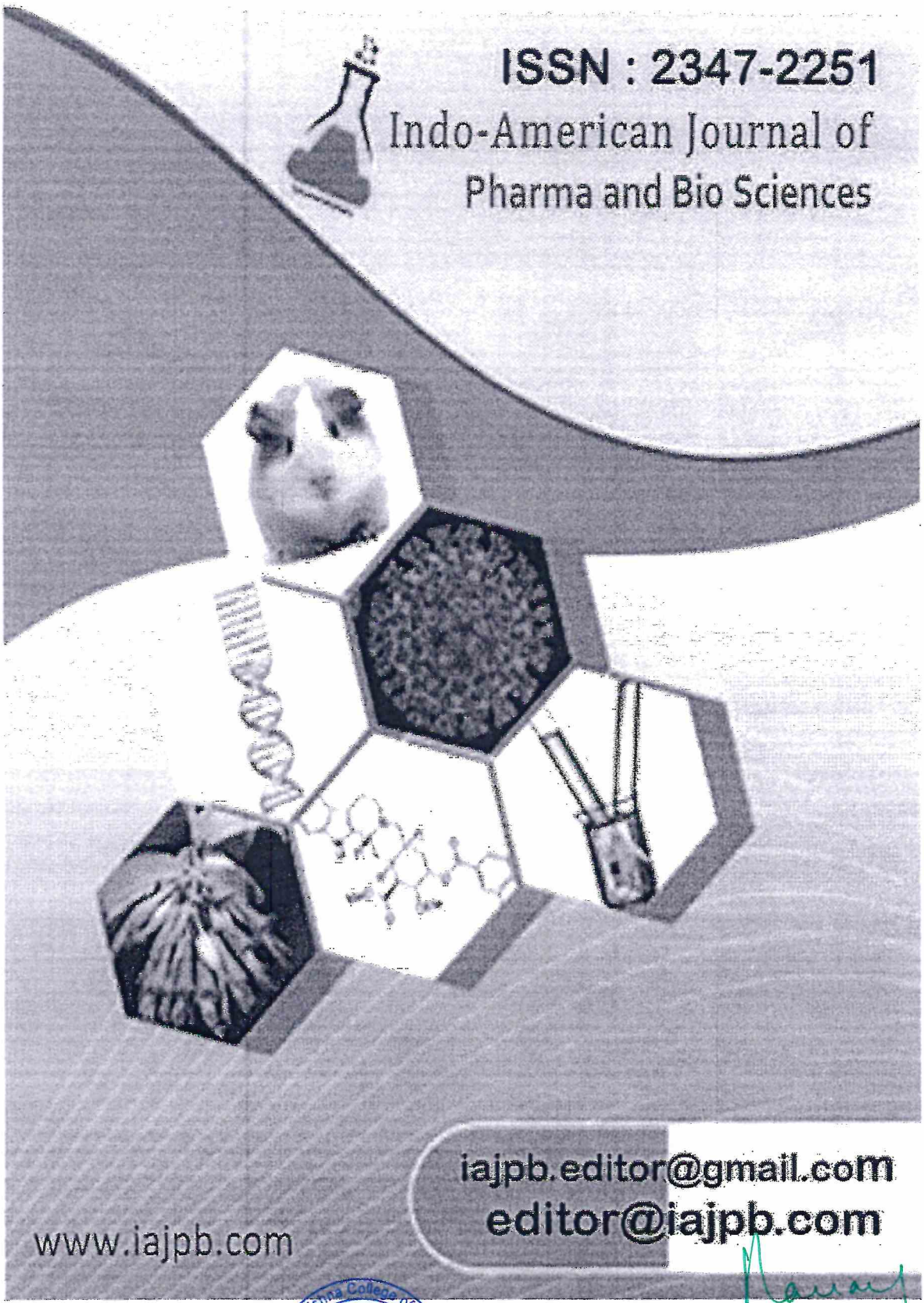

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A STUDY ON SYNTHESIS AND CHARACTERISATION OF SOME NOVEL QUINAZOLINONES

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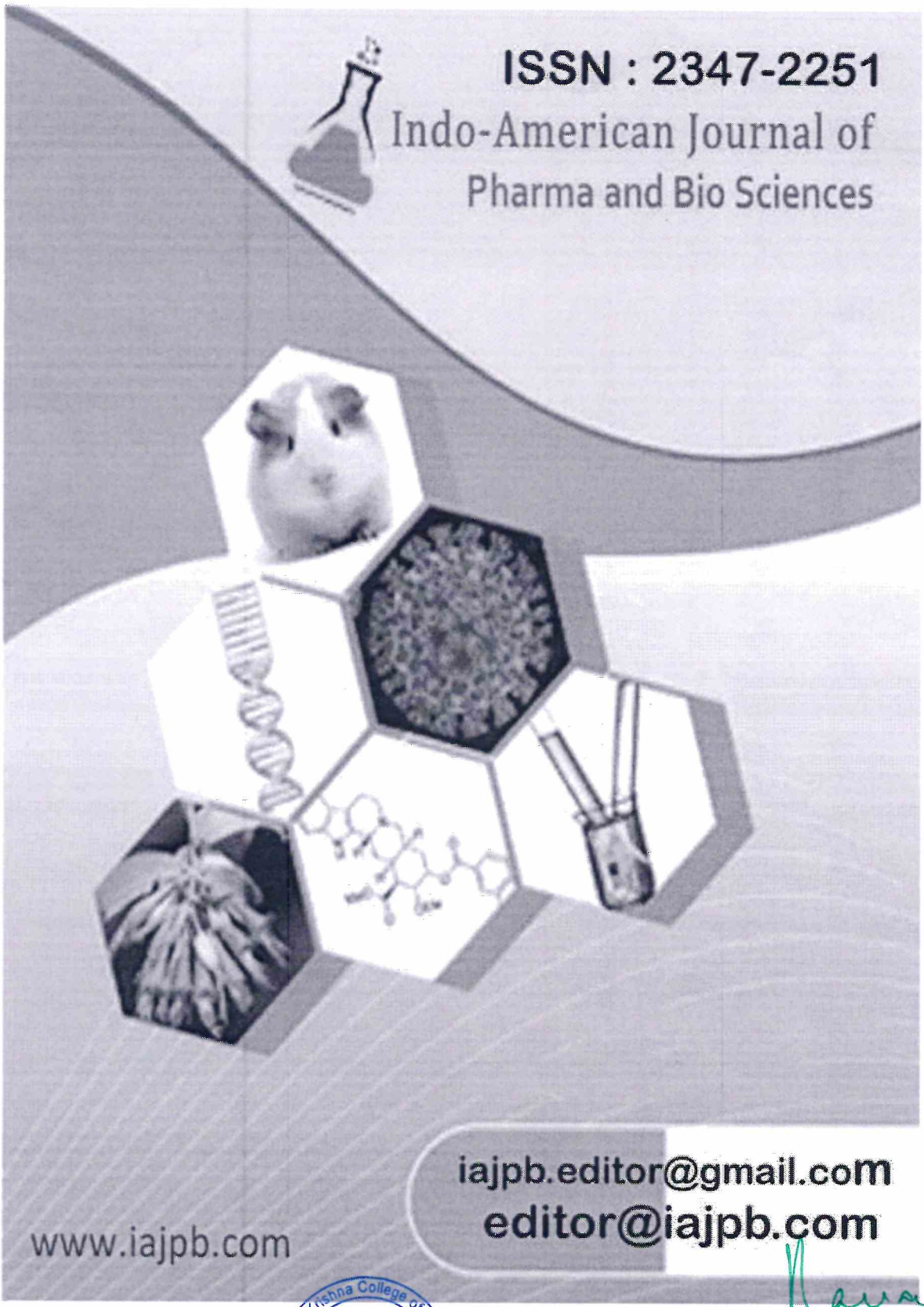
ABSTRACT
Heterocyclic chemistry comprises at least half of all organic chemistry research worldwide. In particular, heterocyclic structures form the basis of many pharmaceutical, agrochemical and veterinary products. The heterocyclic compounds are fundamentals of life, like haeme derivatives in blood & chlorophyll essential for photosynthesis in plants. Also the DNA & RNA are containing heterocycles. The study aims to synthesize simple derivatives of quinazoline by combining with aromatic primary amine, hydrazine hydrate and benzoxazine. The synthesized compounds were characterized by melting point analysis. Melting point was recorded and compared with the standard references. The characterization of compounds provided further scope in the research towards the discovery of new derivatives for several ailments. The biological evaluation could be beneficial for future studies.

KEYWORDS: Heterocyclic compounds, benzoxazine, quinazoline, primary amine, hydrazine hydrate and benzoxazine.

INTRODUCTION
Any of a class of organic compounds whose molecules contain one or more rings of atoms with at least one atom being an element other than carbon, most frequently oxygen, nitrogen, or sulfur are called heterocyclic compounds. Heterocyclic chemistry is the branch of chemistry dealing with the synthesis, properties, and applications of heterocycles. Heterocyclic chemistry comprises at least half of all organic chemistry research worldwide. In particular, heterocyclic structures form the basis of many pharmaceutical, agrochemical and veterinary products. The word hetero means "different from carbon and hydrogen". Many heterocyclic compounds are biosynthesized by plants & animals are biologically active. Some heterocyclic compounds are fundamentals of life, like haeme derivatives in blood & chlorophyll essential for photosynthesis in plants. Also the DNA & RNA are containing heterocycles. Dyestuffs of plant origins include indigo blue used to dye jeans. Several heterocycles are the basic structure nucleus for nicotine, pyridoxine, cocaine, morphine etc. Among a wide variety of nitrogen heterocycles that have been explored for developing pharmaceutically, quinazolinone plays an important role in medicinal chemistry and subsequently has emerged as a pharmacophore. Quinazoline is a compound made up of two fused six member simple aromatic rings- benzene & pyrimidine ring. It is a yellow colored compound, found usually in crystalline form. Medicinally it is used as ant malarial agent. It was first prepared by Gabriel in 1903 and first isolated from the Chinese plant aseru. The development of research on biological activity of quinazolinecompounds started when the compound 2-methyl-1,3-aryl-4-quinazoline was synthesized. This compound has soporific & sedative action.[1-4] In last 10 to 15 years of research for medicinal has been characterized by significant advances. In 1968 only two derivatives were used, soporific & anticonvulsant-methaqualone and diuretic quinathiazone. By 1980, about 50 kinds of derivatives of this class includes medicinal with different biological actions like 'soporific, sedative, tranquilizing, analgesic, anticonvulsant, antitussive, myorelexant, anti rheumatic, hypotensive, antiallergic, bronchodilating, antidiabetic, cholagogue, diuretic, cystatic, antimalarial, spermicidal etc.

Quinazolinone scaffold has been considered as a magic moiety possessing myriad spectrum of medicinal activities. Diversity of biological response profile has attracted considerable interest of several researchers across the globe to explore this skeleton for its assorted



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Pharmacokinetic Variability in Pediatrics and Intensive Care: Toward a Personalized Dosing Approach

Mrs D Kalyani, Ms A R Sridevi , Mrs P Sukanya , Mrs A Aksa anvija , Mr C G Bhaskar

ABSTRACT - Providing a safe and efficacious drug therapy for large and often heterogeneous populations is a challenging objective in clinical drug development and routine clinical practice. It has been known for years that the optimum dose required for many therapeutic agents among individuals is quite variable. A wide interindividual pharmacokinetic variability was described in clinically relevant populations such as pediatrics and critically ill patients. The aim of this article was to present the main individual factors influencing variability in these two populations and their applications. Growth and development are two specific features of children that are not observed in adults. And critically ill patients have a much higher level of sickness severity that is associated with profound pathophysiological changes. These particular features could lead to difficulties to attain therapeutic targets. Nonlinear mixed effects modeling is a common approach to identify unexplained population variability. This approach is often applied to evaluate and optimize drug therapy in particular populations. Numerous studies have been conducted in these two specific populations to characterize pharmacokinetic parameters and to identify individual factors influencing variability. Size, age and organ function appeared to be the main factors influencing pharmacokinetics in pediatrics. Factors influencing pharmacokinetics in critically ill patients were mainly cardiovascular system, organ dysfunction and organ support. Dosage individualization seems to be a key issue to optimize drug treatment in these specific populations. Clinically utility and safety of a model-based personalized drug therapy has been demonstrated for vancomycin in pediatrics. Many programs were available to optimize drug regimens, especially for antibiotic drugs in critically ill patients. This innovative personalized dosing approach is a promising way to optimize drug therapy in clinically relevant populations, such as pediatrics and critically ill patients.

INTRODUCTION

Providing a safe and efficacious drug therapy for large and often heterogeneous populations is a challenging objective in clinical drug development and routine clinical practice. On the one hand, a therapeutic effect of the drug is desired to be achieved for all patients; on the other hand too high concentrations have to be avoided to reduce adverse events [1,2]. It has been known for years that the optimum dose required for many therapeutic agents among individuals is quite variable. Anatomical and physiological properties have a great influence on the pharmacokinetics of drugs and lead to inter- and intra-individual variability in the pharmacokinetics outcome [3]. Both inter- and intrasubject pharmacokinetic variability may be important. Intersubject variability is fundamental to the argument for using A wide interindividual pharmacokinetic variability was described in clinically relevant populations such as pediatrics and critically ill patients. Growth and development are two specific features of children that are not observed in adults. And critically ill patients have a much higher level of sickness severity that is associated with profound pathophysiological changes. These particular features could lead to difficulties to attain therapeutic targets.One well-known approach to characterize variability in pharmacokinetic parameters is nonlinear mixed effects modeling. It is a common approach to identify unexplained population variability in parameters of pharmacokinetic models and to identify covariates, which explain the variability of the data. Population models can then be developed using bayesian logistics to therapeutic drug monitoring.

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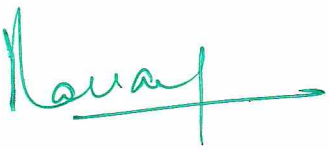

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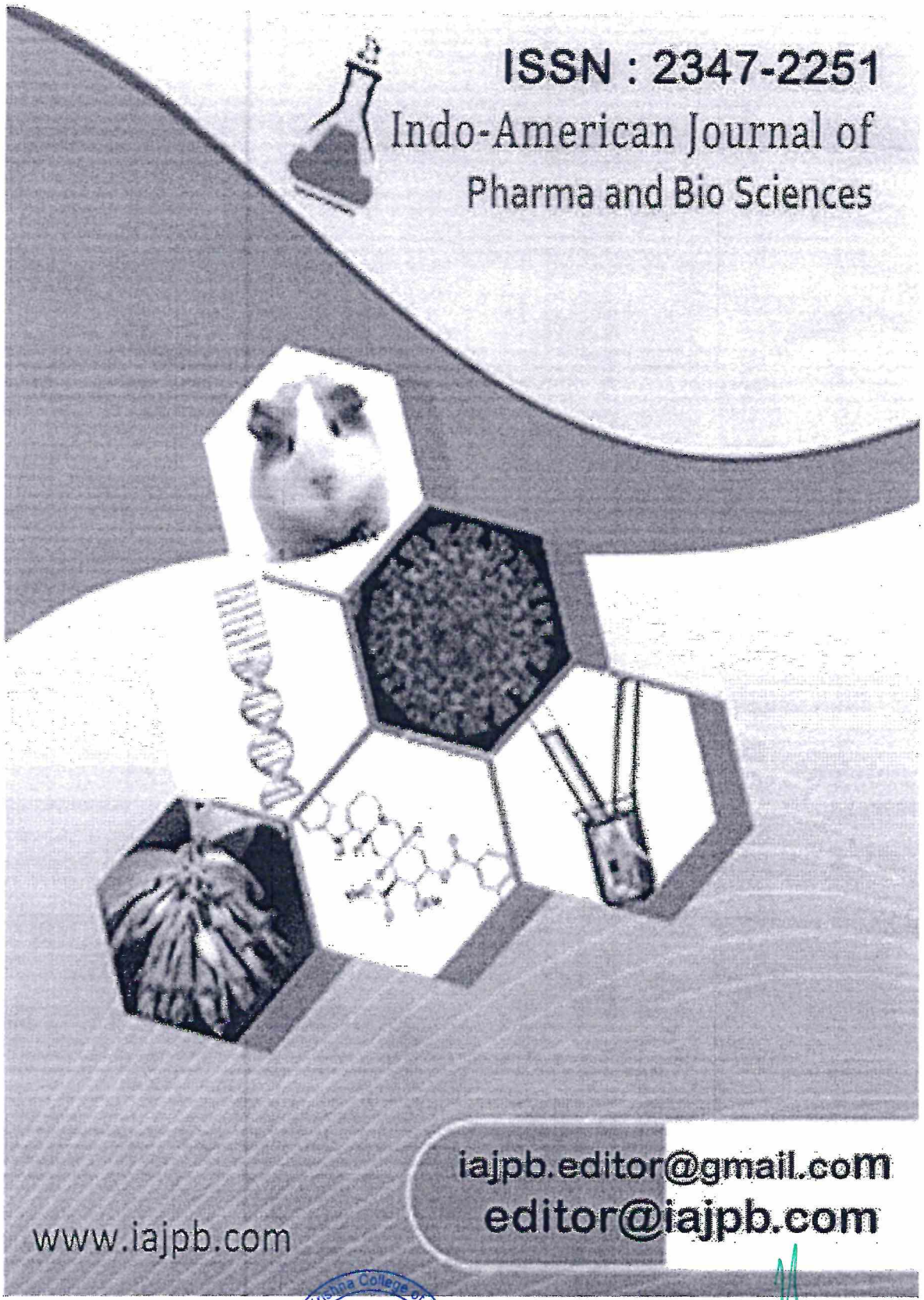

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Indo-American Journal of Pharma and Bio Sciences

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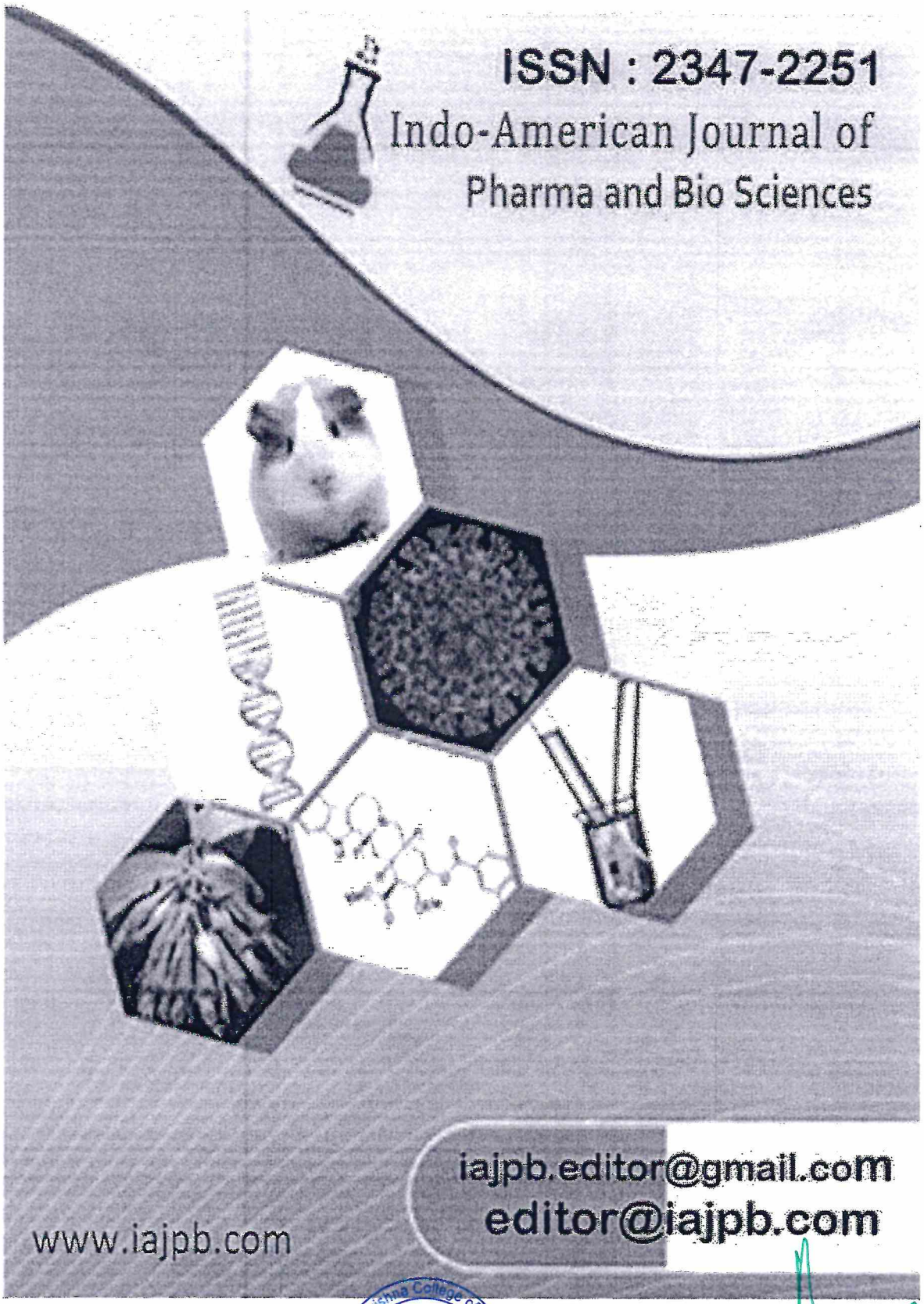

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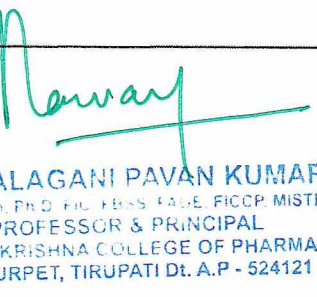

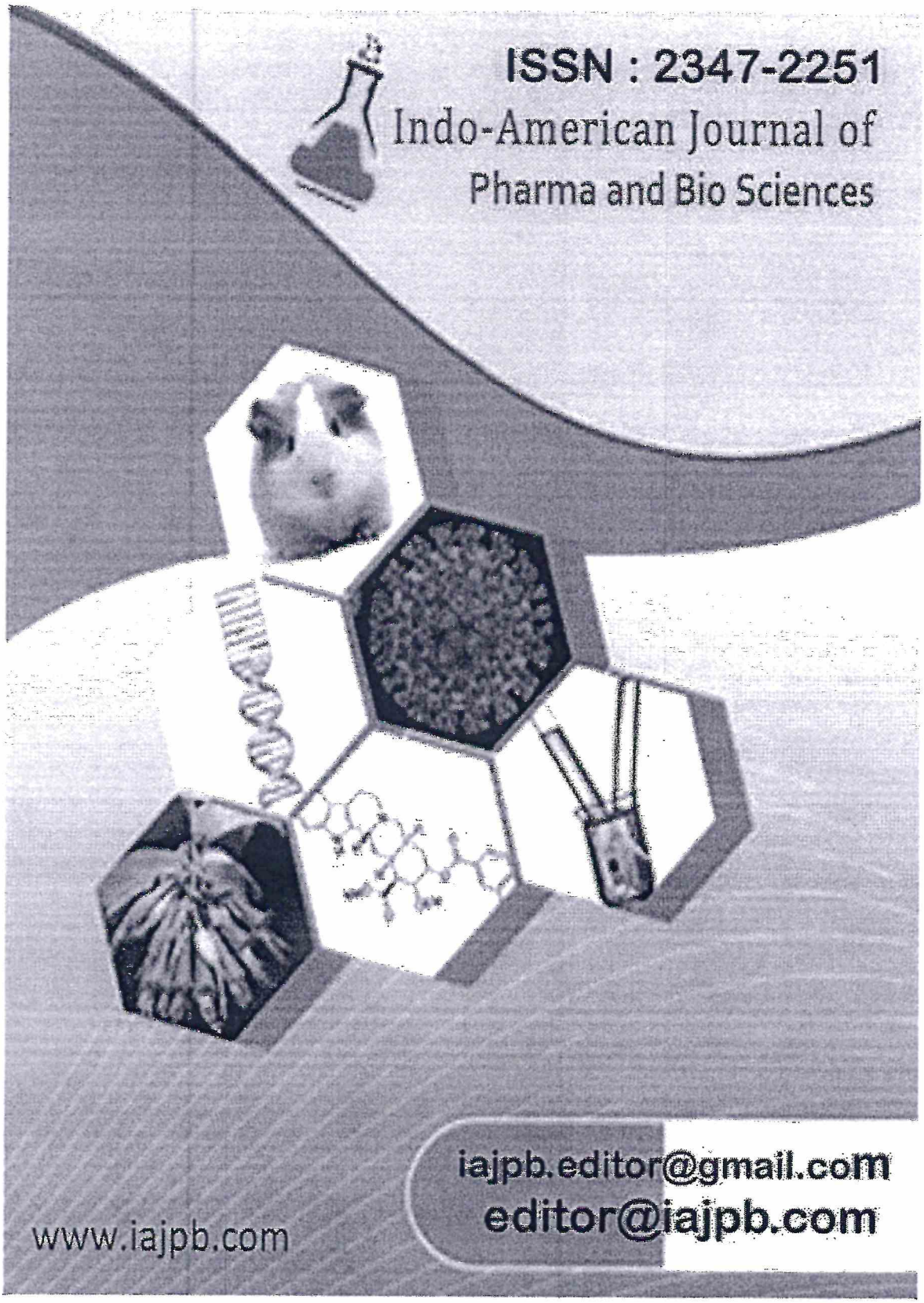

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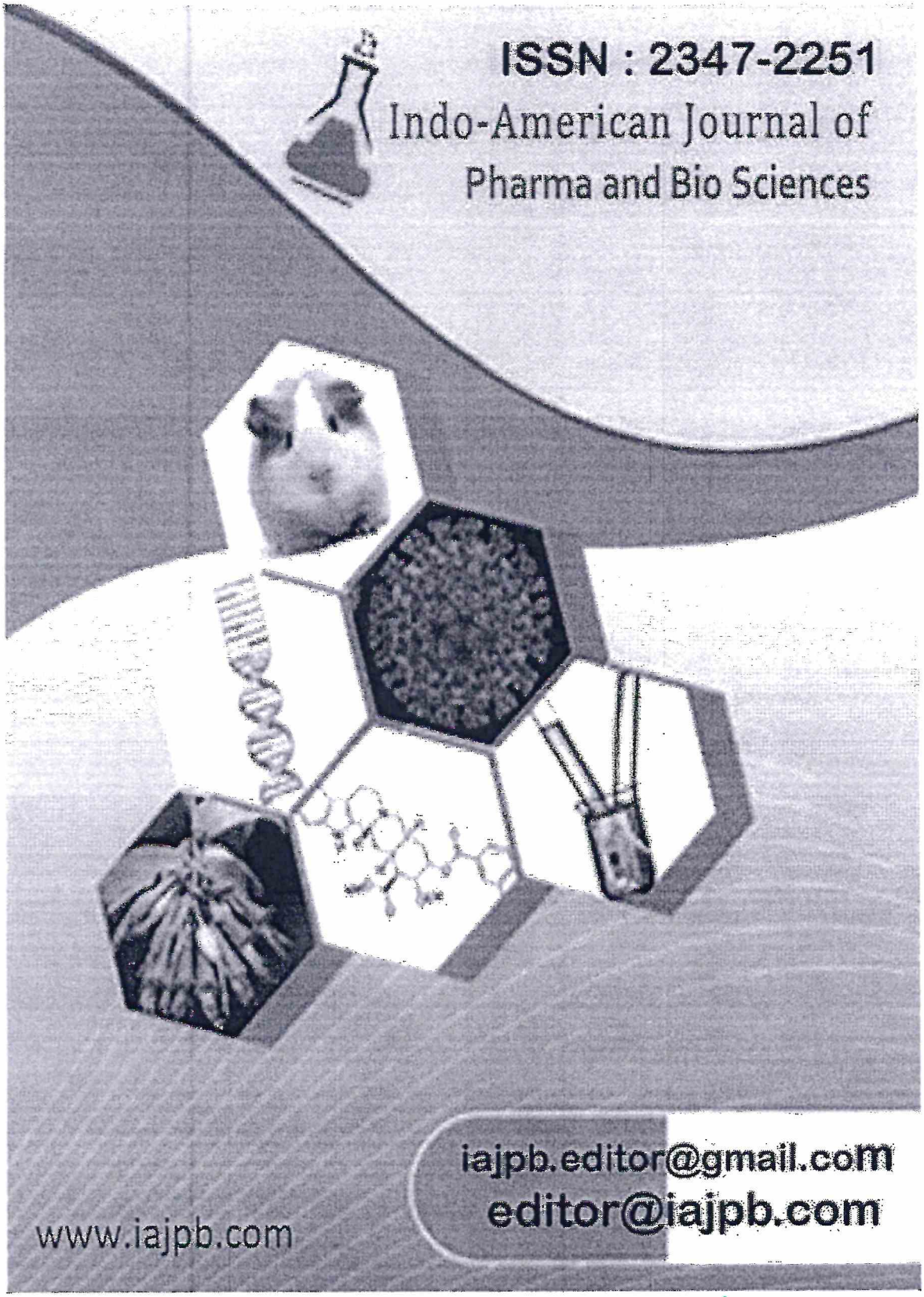

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Mrs D Kalyani , Mrs T Swathi , Mrs P Sukanya , Mrs CH Harika , Mrs K Vanitha Devi

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The Sensitive Method of Subvisible Particle Counting for the Detection and Quantification of Monoclonal Antibody Aggregation Caused by Freeze-Thawing: New Understanding of Particle Function in the Protein Aggregation Process

Mrs N Sukanya , Mrs P K Devibala , Ms.SK Zoofishaan , Mr.M R Pavan Kumar , Mr S Sivakoteswa Rao

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Cytotoxic Compounds from *Kibatalia gitingensis* (Elm.) Woodson

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ABSTRACT

The cytotoxic activities of ursolic acid (1), squalene (2), a mixture of α-amyrin acetate (3a) and lupeol acetate (3b), and isoscopoletin (4), which were extracted from the dichloromethane extracts of Kibatalia gitingensis's leaves and twigs, were tested against three human cancer cell lines: MCF-7 for breast cancer, HT-29 and HCT-116 for colon cancer, and HDFn, a normal cell line, using the in vitro PrestoBlue® cell viability assay. The IC50 values for compounds 1-4 ranged from 0.6931 to 1.083 µg/mL, indicating high cytotoxic effects against HT-29 cells. In addition, the IC50 values for 1-4 ranged from 4.065 to 11.09 µg/mL, indicating significant cytotoxicity against HCT-116 cells.

The MCF-7 cells were least affected by these substances, with IC50 values varying between 8.642 and 25.87 µg/mL. On the one hand, 2, 4 and 1, respectively, are the most cytotoxic to HT-29 cells, HCT-116 cells, and MCF-7 cells.

Key words: Subfamily Apocynaceae, Kibatalia gitingensis Cytotoxicity, MCF-7, HCT-116, HT-29, HDFn, ursolic acid, squalene, α-amyrin acetate, Lupeol acetate, isoscopoletin, and PrestoBlue® cell viability test.

INTRODUCTION

Local names for the Apocynaceae family member Kibatalia gitingensis (Elm.) Woodson include "laniti" and "laneteng-gubat" in the Philippines. According to the International Union for the Conservation of Nature's Red List of Threatened Species, it is considered susceptible to extinction.The alkaloid concentration gives it therapeutic benefits, and it is also widely utilized as a construction material and for ornamental carvings.gitingensine, a steroidal alkaloid isolated from K. gitingensis leaves, has ataraxic effects (the ability to relax smooth muscles) and antispasmodic activity (the ability to widen the arteries of skeletal muscles and the splanchnic area).5 Kibataline6,7 and 20-(epi-N-methyl) paravallarine were found in K. gitingensis leaves in other research.8 The azasteroidal alkaloid found in the plant eliminated serotonin-induced spasms and stimulated spontaneous movement in canines and mice.Paravallarine, N-methylparavallarine, and 20-epiparavallarine are among the several alkaloids extracted from K. gitingensis bark.Not only that, but lanitine (2α-hydroxy- N-methylparavallarine) and its 2β-isomer were found in the plant's stem bark, according to reports.11

Our ongoing investigation into the bioactivities and chemical compositions of native and indigenous Philippine plants includes this study. In a previous paper, we detailed the procedure for extracting and identifying ursolic acid (1), squalene (2), a combination of α-amyrin acetate (3a) and lupeol acetate (3b) from the leaves, and 1-3 and isoscopoletin.

MATERIALS AND METHODS

Sample Collection

Samples of leaves and twigs of *Kibatalia gitingensis*(Elm.) Woodson were collected from the De La Salle University–Science and Technology Complex (DLSU-STC) reforested area in February 2014. The samples were authenticated and deposited at the De La Salle University Herbarium with voucher specimen#908.

Isolation and Structure Elucidation

The isolation and structure elucidation of **1-4** from the leaves and twigs of *K. gitingensis* were reported previously.[12]

Preparation of Compounds forCytotoxicity Tests

The compounds (**1-4**) from *K. gitingensis* were dissolved in dimethyl sulfoxide (DMSO) to makea 4 mg/mL stock solution. Working solutions were prepared in complete growth medium to a final non-toxic DMSO concentration of 0.1%.

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Cytotoxic Compounds from *Kibatalia gitingensis* (Elm.) Woodson

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ABSTRACT

The cytotoxic activities of ursolic acid (1), squalene (2), a mixture of α-amyrin acetate (3a) and lupeol acetate (3b), and isoscopoletin (4), which were extracted from the dichloromethane extracts of Kibatalia gitingensis's leaves and twigs, were tested against three human cancer cell lines: MCF-7 for breast cancer, HT-29 and HCT-116 for colon cancer, and HDFn, a normal cell line, using the in vitro PrestoBlue® cell viability assay. The IC50 values for compounds 1-4 ranged from 0.6931 to 1.083 µg/mL, indicating high cytotoxic effects against HT-29 cells. In addition, the IC50 values for 1-4 ranged from 4.065 to 11.09 µg/mL, indicating significant cytotoxicity against HCT-116 cells.

The MCF-7 cells were least affected by these substances, with IC50 values varying between 8.642 and 25.87 µg/mL. On the one hand, 2, 4 and 1, respectively, are the most cytotoxic to HT-29 cells, HCT-116 cells, and MCF-7 cells.

Key words: Subfamily Apocynaceae, Kibatalia gitingensis Cytotoxicity, MCF-7, HCT-116, HT-29, HDFn, ursolic acid, squalene, α-amyrin acetate, Lupeol acetate, isoscopoletin, and PrestoBlue® cell viability test.

INTRODUCTION

Local names for the Apocynaceae family member Kibatalia gitingensis (Elm.) Woodson include "laniti" and "laneteng-gubat" in the Philippines. According to the International Union for the Conservation of Nature's Red List of Threatened Species, it is considered susceptible to extinction.The alkaloid concentration gives it therapeutic benefits, and it is also widely utilized as a construction material and for ornamental carvings.gitingensine, a steroidal alkaloid isolated from K. gitingensis leaves, has ataraxic effects (the ability to relax smooth muscles) and antispasmodic activity (the ability to widen the arteries of skeletal muscles and the splanchnic area).5 Kibataline6,7 and 20-(epi-N-methyl) paravallarine were found in K. gitingensis leaves in other research.8 The azasteroidal alkaloid found in the plant eliminated serotonin-induced spasm and stimulated spontaneous movement in canines and mice.Paravallarine, N-methylparavallarine, and 20 epiparavallarine are among the several alkaloids extracted from K. gitingensis bark.Not only that, but lanitine (2α-hydroxy- N methylparavallarine) and its 2β-isomer were found in the plant's stem bark, according to reports.11

Our ongoing investigation into the bioactivities and chemical compositions of native and indigenous Philippine plants includes this study. In a previous paper, we detailed the procedure for extracting and identifying ursolic acid (1) squalene (2), a combination of α-amyrin acetate (3a) and lupeol acetate (3b) from the leaves, and 1-3 and isoscopoletin.

MATERIALS AND METHODS

Sample Collection

Samples of leaves and twigs of *Kibatalia gitingensis* (Elm.) Woodson were collected from the De La Salle University–Science and Technology Complex (DLSU-STC) reforested area in February 2014. The samples were authenticated and deposited at the De La Salle University Herbarium with voucher specimen#908.

Isolation and Structure Elucidation

The isolation and structure elucidation of **1-4** from the leaves and twigs of *K. gitingensis* were reported previously.[12]

Preparation of Compounds forCytotoxicity Tests

The compounds (**1-4**) from *K. gitingensis* were dissolved in dimethyl sulfoxide (DMSO) to makea 4 mg/mL stock solution. Working solutions were prepared in complete growth medium to a final non-toxic DMSO concentration of 0.1%.

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Development and Standardization of a Polyherbal Anti Urolithiatic Suspension

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Urolithiasis,
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Antilithiatic Effect,
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Cystone

ABSTRACT

Renal terrific concentration with respect to stone forming components is mostly recognized to become one of the casual factors such as Calculogenisis. At this work, the preparation and standardization of polyherbal suspension was carried out. Proximate analysis values include percentage of the overall residue, proportion like acetone non-soluble residue, fraction of water soluble ash, percentage of moisture content and percentage of extractive values were analysed for various plants. Preliminary phytochemical analysis of various extracts of the plant revealed the presence of various constituents like glycosides, flavonoids, saponins, steroids etc. Poly-herbal anti-urolithiatic suspension was prepared by combining the prepared extracts of *Tribulus terrestris* L., *Aerva lanata* L., *Crataeva religiosa* Hook & Frost and *Emblica officinalis* L. with suspension base. The prepared formulation showed good stability and redispersibility.Inside the research project, male mice have been chosen to urolithiasis so because excretory system of male mice starts to resemble that from people and then also existing research show that having the quantity like stone discharge through female mice had been substantially lower. Such research results, thereby stimulate the need for any further research to hold over the antilithiatic effect of the polyherbal suspension to prove that more effective treatment for lithiasis with polyherbal suspension can be achieved.

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INTRODUCTION

Urolithiasis is a condition where stones form in the kidneys or the bladder. These stones are made of minerals and salts. Patients with this condition can have a variety of symptoms, depending on how severe it is. Urinary stones are calcifications that form in the kidney, ureter, or bladder [1]. They are most common in children and older adults. Urinary stones can be just like a little like a dust particle or even as big as either a tennis ball. Symptoms of urinary stones include blood in your urine, an inability to urinate, pain when urinating, increased thirst and dark urine. If untreated there is a high risk for acute renal failure resulting in kidney problems [2]. Urolithiasis is a medical term for bladder, kidney or

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2	An Investigation of Effectiveness of Aluminium chloride induced Alzhemer's disease in various Experimental Rats	P.Kavitha	Asian Journal of Phytomedicine and Clinical Research	2321-0915
3	UV/VIS imaging-based PAT tool for drug particle size inspection in intact tablets supported by pattern recognition neural networks	Dr.Balagani Pavan Kumar	Indo-American Journal of Pharma and Biosciences	2347-2251
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7	UV/VIS imaging-based PAT tool for drug particle size inspection in intact tablets supported by pattern recognition neural networks	Mr.N Praveen Kumar	Indo-American Journal of Pharma and Biosciences	2347-2251
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24	The Synthesis of Diverse Annulated Pyridines with 6-Membered Functionalized Saturated Cycles for Medical Chemistry Research	Dr.C Rajaram	International Journal of Pharmaceutical Sciences Letters	2277-2685
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27	The Synthesis of Diverse Annulated Pyridines with 6-Membered Functionalized Saturated Cycles for Medical Chemistry Research	Mr Y Naveen Kumar	International Journal of Pharmaceutical Sciences Letters	2277-2685
28	A randomised, parallel, open-label clinical study comparing the effectiveness and safety of apremilast with methotrexate in individuals with moderate to severe palmoplantar psoriasis.	Mrs T Swathi	International Journal of Pharmaceutical Sciences Letters	2277-2685

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AN INVESTIGATION OF EFFECTIVENESS OF ALUMINIUM CHLORIDE INDUCED ALZHEIMER'S DISEASE IN VARIOUS EXPERIMENTAL RATS

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ABSTRACT

The Neuroprotective against $AlCl_3$ induced toxicity. Enhanced learning and memory was allied to ingestion of extract in rats. Al overload, AChE hyperactivity are responsible for alzheimers disease which are neutralized or reduced with treatment of extract, which might be due to the synergistic action of its active constituents. However extensive research is needed to validate the anti-alzheimeric effect of extract active components against a variety of models of AD, prior to entering into the clinical trials.

KEYWORDS

Anti-alzheimeric effect, $AlCl_3$ and AChE hyperactivity.

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INTRODUCTION

As of 2020 globally, there were approximately 51 million people worldwide with Alzheimer's disease. It most often begins in people over 65 years of age, although up to 11% of cases are early-onset affecting those in their 30s to mid 60s. Women get sick more often than men. It affects about 6% of people 65 years and older[1]. In 2015, all forms of dementia resulted in about 1.9 million deaths.

Causes

Less than 1% of the time, Alzheimer's is caused by specific genetic changes that virtually guarantee a person will develop the disease.

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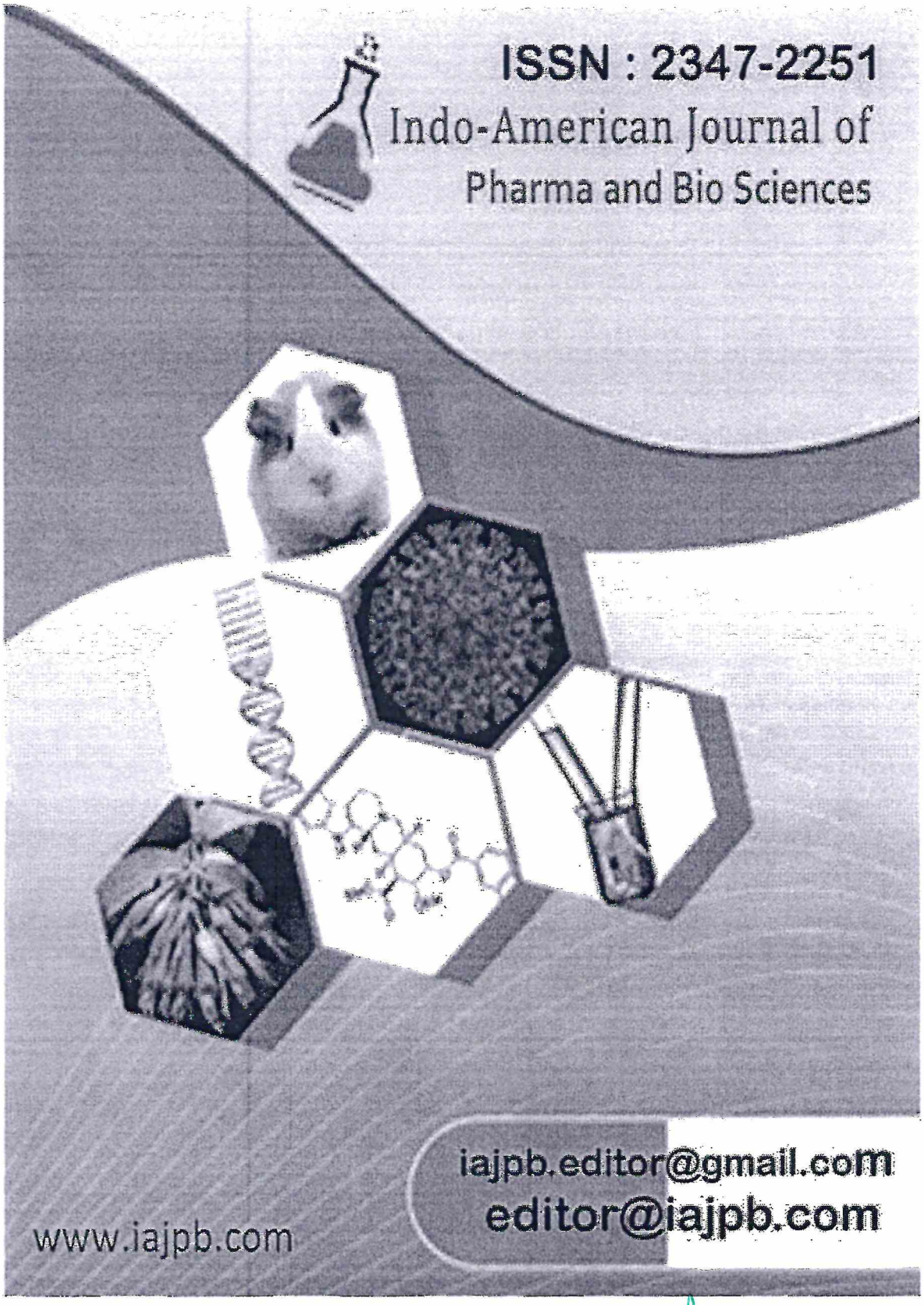

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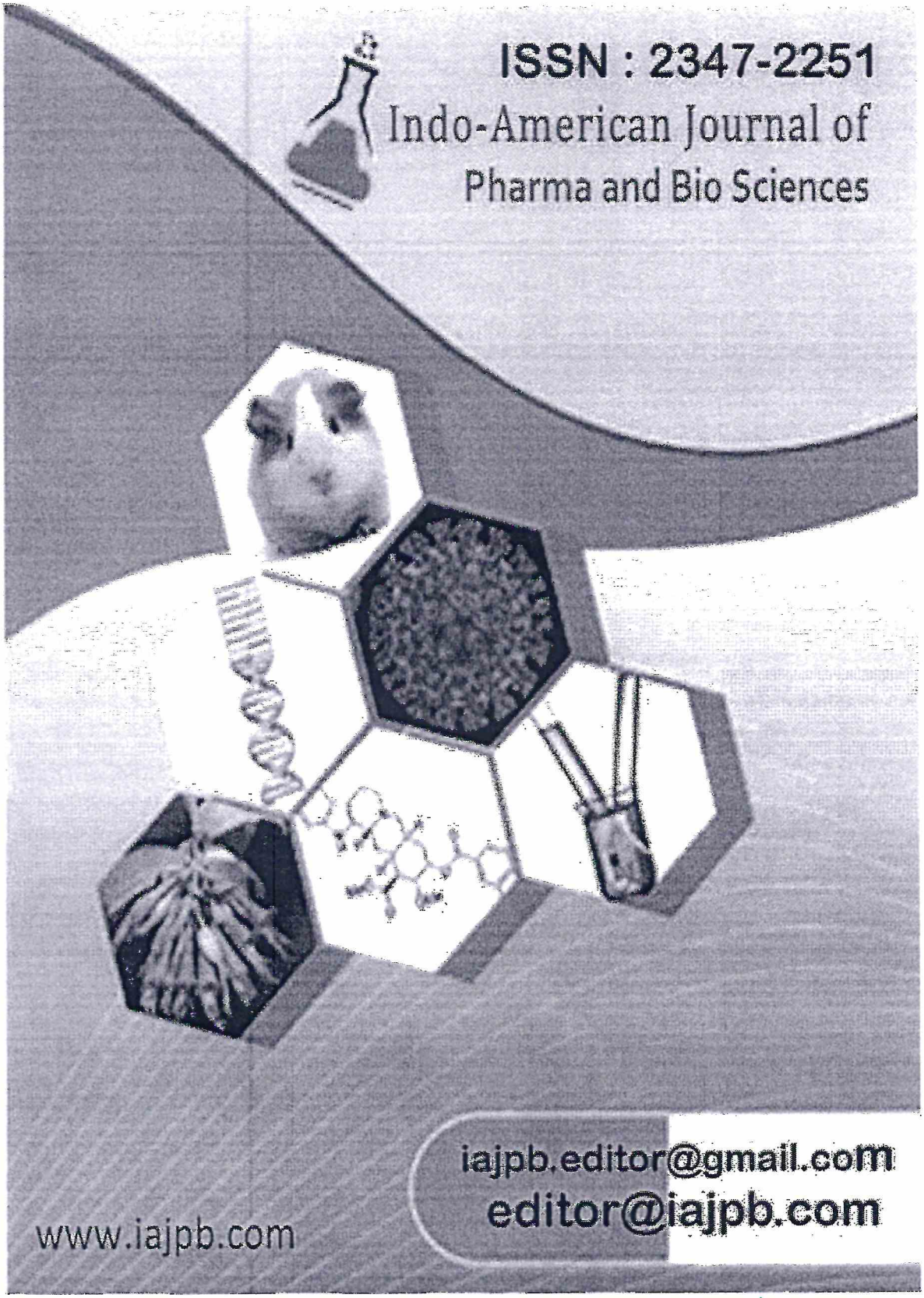

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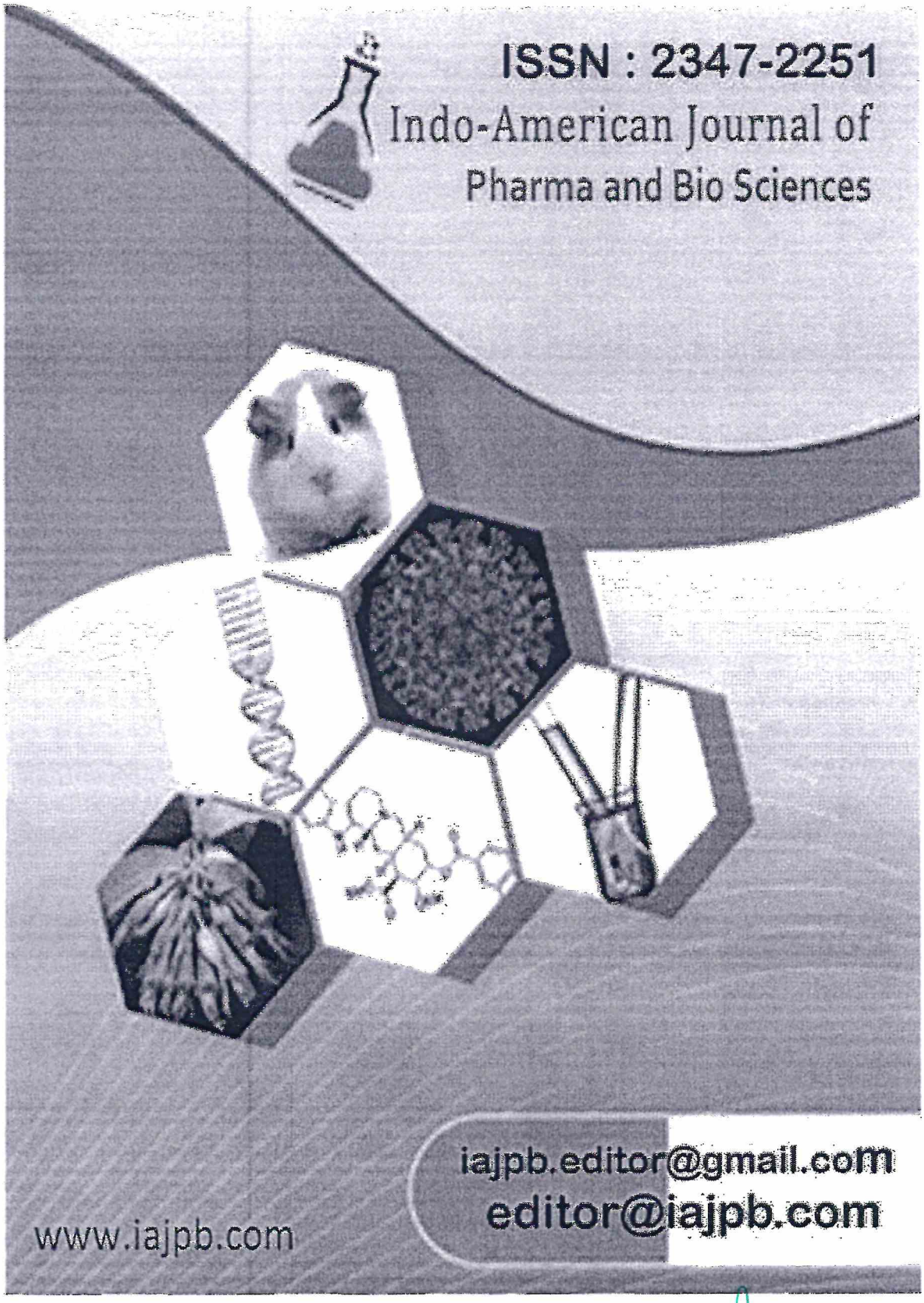

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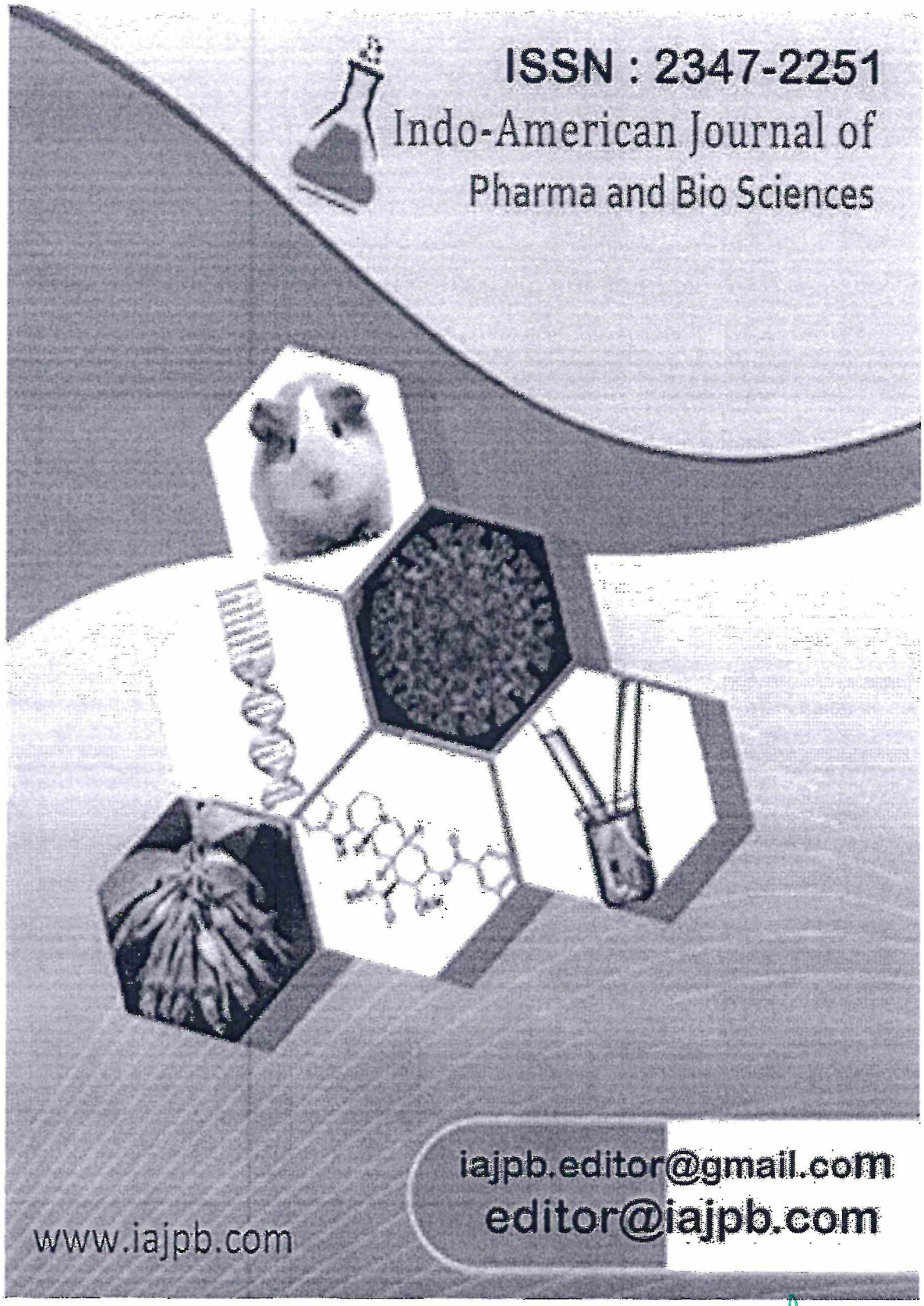

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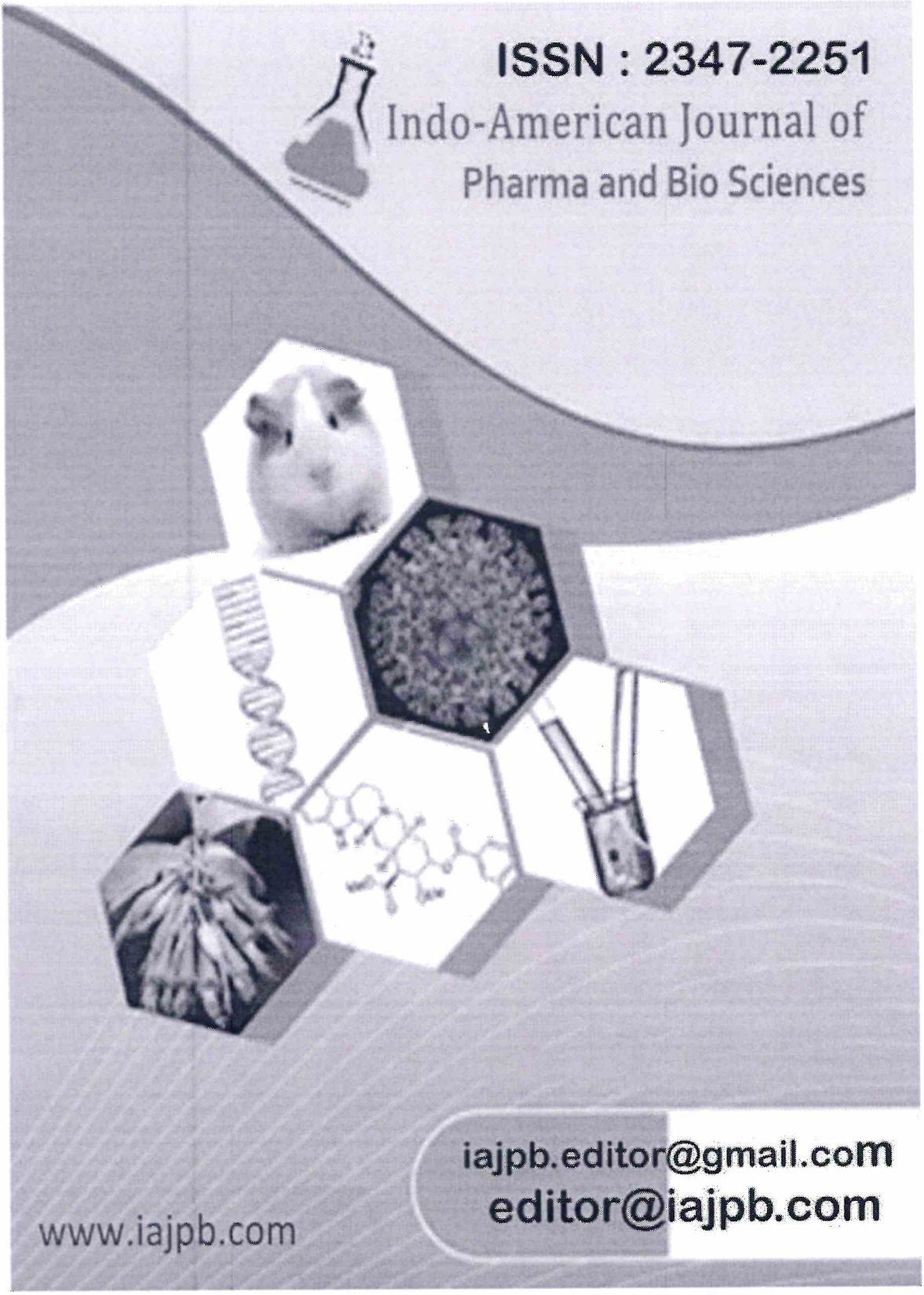

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Screening of Antidepressant Activity of *Punica granatum* in Mice

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ABSTRACT

Introduction: There are many different mental health issues, including depression, that may be alleviated with the use of the medicinal plants found in India. Acute and chronic administration of Punica granatum (pomegranate) whole fruit had an antidepressant effect on rats, which was the aim of this research. We employed an oral regimen of Punica granatum aqueous extract (250 and 500 mg/kg daily), imipramine (10 mg/kg), and gum acacia (10 ml/kg) as a carrier. Each of the four animal groupings consisted of six creatures. The acute study required the administration of medicines or vehicles 60 minutes before the experiments began. All medications and vehicles used in the long-term trial were given for a total of 14 days, with the last dosage given 60 minutes before the experiment on day 14. To evaluate the efficacy of antidepressants, researchers used the Forced Swim Test and the Tail Suspension Test. An analysis of variance (ANOVA) was performed on the data, with drug therapy being the independent variable. We used Dunnett's test to do post hoc comparisons. The results showed that the period of immobility was greatly decreased in the acute tail suspension test, chronic forced swim test, and acute swim test by the PG 500 mg/kg group, but not in the 250 mg/kg group. The groups treated with PG 250 mg/kg and 500 mg/kg showed a significant reduction in the duration of immobility in the chronic tail suspension test. At 500 mg/kg, the antidepressant effect was similar to that of 10 mg/kg of imipramine. In conclusion, this research provides further evidence that 500 mg/kg of aqueous extract of entire P. granatum fruit has antidepressant effect. Given the nutritional and functional benefits of pomegranate extract, it would be wise to recommend its use to patients suffering from depression.

Key words: Feeling down, tests for tail suspension and forced swimming, pomegranate.

INTRODUCTION

Depression is a long-term mental health condition that may strike anybody at any time. The existing arsenal of treatment is often insufficient, with disappointing outcomes in around one-third of all people treated, despite the availability of numerous powerful antidepressants.1 This gives researchers a reason to keep looking for better antidepressants. There are now more options for treating depression than the currently available synthetic medications due to their limitations. Herbal medicines are an example of an old therapy that has persisted over the years since plants have always been a source of medications. Pomegranate, scientifically known as Punica granatum L. (PG), is a popular fruit and juice variety. The Punicaceae family includes it. The Himalayas in northern India are its natural habitat. From ancient times, it has been farmed all throughout the Mediterranean.2 Valuable chemicals are found in several portions of the pomegranate fruit, including the skin, seeds, and arils. The peel contains a myriad of compounds and minerals, including gallic acid, ellagic acid, catechin, epicatechin, epigallocatechin-3-gallate, quercetin, kaempferol, luteolin, rutin, kaempferol-3-O-glycoside, gallagyldilacton, pedunculagin, tellima-grandin, and many more. The seeds contain punicic acid, linoleic acid, oleic acid, palmitic acid, stigmasterol, β-sitosterol, dau-costerol, camesterol, cholesterol, estriol, estrone, estriol, estriol, tocopherols, ursolic acid, oleanolic acid, isoflavones, and phenyl aliphatic glycosides/lignins, among other major chemical components. The components found in the aril include sugars, pectin, polyphenols, anthocyanins, fatty acids, amino and organic acids, indoleamines, sterols, triterpenoids, and α-tocopherol.3,4

In traditional medicine, pomegranate is used to cure a variety of conditions, including parasite infestations, diarrhea, acidosis, dysentery, bleeding, microbiological infections, respiratory disorders, and aphthus ulcers. It is also used as an antipyretic and vermifuge.5 Various components of the P. granatum fruit have shown anti-inflammatory, anti-cancer, anti-tumor, antihepatotoxic, anti-Diabetic, and antiatherogenic3 characteristics. Reportedly, it also helps with Alzheimer's illness.3, 7 Juice, wine,8 dried arils9, and jam are just a few examples of PG-based products that have been the subject of academic investigation.10 Despite this, research on the health benefits of P. granatum in its entire fruit form is limited. It is possible that the combined effect of the fruit's components is more effective than the sum of its parts. The central nervous system (CNS) effects of P. granatum have received little attention, and the antidepressant effects of the whole fruit have not been documented. Therefore, the purpose

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Introduction: There are many different mental health issues, including depression, that may be alleviated with the use of the medicinal plants found in India. Acute and chronic administration of Punica granatum (pomegranate) whole fruit had an antidepressant effect on rats, which was the aim of this research. We employed an oral regimen of Punica granatum aqueous extract (250 and 500 mg/kg daily), imipramine (10 mg/kg), and gum acacia (10 ml/kg) as a carrier. Each of the four animal groupings consisted of six creatures. The acute study required the administration of medicines or vehicles 60 minutes before the experiments began. All medications and vehicles used in the long-term trial were given for a total of 14 days, with the last dosage given 60 minutes before the experiment on day 14. To evaluate the efficacy of antidepressants, researchers used the Forced Swim Test and the Tail Suspension Test. An analysis of variance (ANOVA) was performed on the data, with drug therapy being the independent variable. We used Dunnett's test to do post hoc comparisons. The results showed that the period of immobility was greatly decreased in the acute tail suspension test, chronic forced swim test, and acute swim test by the PG 500 mg/kg group, but not in the 250 mg/kg group. The groups treated with PG 250 mg/kg and 500 mg/kg showed a significant reduction in the duration of immobility in the chronic tail suspension test. At 500 mg/kg, the antidepressant effect was similar to that of 10 mg/kg of imipramine. In conclusion, this research provides further evidence that 500 mg/kg of aqueous extract of entire P. granatum fruit has antidepressant effect. Given the nutritional and functional benefits of pomegranate extract, it would be wise to recommend its use to patients suffering from depression.

Key words: Feeling down, tests for tail suspension and forced swimming, pomegranate.

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Depression is a long-term mental health condition that may strike anybody at any time. The existing arsenal of treatment is often insufficient, with disappointing outcomes in around one-third of all people treated, despite the availability of numerous powerful antidepressants.1 This gives researchers a reason to keep looking for better antidepressants. There are now more options for treating depression than the currently available synthetic medications due to their limitations. Herbal medicines are an example of an old therapy that has persisted over the years since plants have always been a source of medications. Pomegranate, scientifically known as Punica granatum L. (PG), is a popular fruit and juice variety. The Punicaceae family includes it. The Himalayas in northern India are its natural habitat. From ancient times, it has been farmed all throughout the Mediterranean.2 Valuable chemicals are found in several portions of the pomegranate fruit, including the skin, seeds, and arils. The peel contains a myriad of compounds and minerals, including gallic acid, ellagic acid, catechin, epicatechin, epigallocatechin-3-gallate, quercetin, kaempferol, luteolin, rutin, kaempferol-3-O-glycoside, gallagyldilacton, pedunculagin, tellimagrandin, and many more. The seeds contain punicic acid, linoleic acid, oleic acid, palmitic acid, stigmasterol, β-sitosterol, dau-costerol, camesterol, cholesterol, estriol, estrone, estriol, estriol, tocopherols, ursolic acid, oleanolic acid, isoflavones, and phenyl aliphatic glycosides/lignins, among other major chemical components. The components found in the aril include sugars, pectin, polyphenols, anthocyanins, fatty acids, amino and organic acids, indoleamines, sterols, triterpenoids, and α-tocopherol.3,4

In traditional medicine, pomegranate is used to cure a variety of conditions, including parasite infestations, diarrhea, acidosis, dysentery, bleeding, microbiological infections, respiratory disorders, and aphthus ulcers. It is also used as an antipyretic and vermifuge.5 Various components of the P. granatum fruit have shown anti-inflammatory, anti-cancer, anti-tumor, antihepatotoxic, anti-Diabetic, and antiatherogenic3 characteristics. Reportedly, it also helps with Alzheimer's illness.3, 7 Juice, wine,8 dried arils9, and jam are just a few examples of PG-based products that have been the subject of academic investigation.10 Despite this, research on the health benefits of P. granatum in its entire fruit form is limited. It is possible that the combined effect of the fruit's components is more effective than the sum of its parts. The central nervous system (CNS) effects of P. granatum have received little attention, and the antidepressant effects of the whole fruit have not been documented. Therefore, the purpose

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Screening of Antidepressant Activity of *Punica granatum* in Mice

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Abstract

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INTRODUCTION

In order to stimulate an adequate immune response, adjuvants are necessary for vaccines that include recombinant proteins.1, 2 The only adjuvants used in U.S.-approved vaccinations that are now available for purchase are aluminum hydroxide, aluminum phosphate, and aluminum salt adjuvants. In contrast to aluminum phosphate, which has a plate-like molecular structure, aluminum hydroxide, also known as boehmite (AlOOH),3 is composed of needle-like particles with sizes of 2 nm. main particles in the 50 nm range and their phology.5 When combined in a solution, the two adjuvants produce stable porous aggregates with a diameter of 1–10 mm.4,5 Several factors are likely responsible for the incompletely known mechanisms of action of aluminum salt adjuvants.

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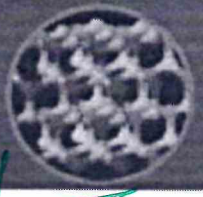

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The Developability Classification System: Application of Biopharmaceutics Concepts to Formulation Development

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ABSTRACT: A revised classification system for oral drugs was developed using the biophar- maceutics classification system (BCS) as a starting point. The revised system is designed to have a greater focus on drug developability. Intestinal solubility, the compensatory nature of solubility and permeability in the small intestine and an estimate of the particle size needed to overcome dissolution rate limited absorption were all considered in the revised system. The system was then validated by comparison with literature on the *in vivo* performance of a number of test compounds. Observations on the test compounds were consistent with the revised classification, termed the developability classification system (DCS), showing it to be of greater value in predicting what factors are critical to *in vivo* performance than the widely used BCS.

INTRODUCTION

Following its introduction in the 1990s, the biopharmaceutics categorization system (BCS) had a significant impact on the creation of oral dosage forms with instant release (IR). This method replaced in vivo human trials with in vitro data to prove bioequivalence of low risk (BCS class I) chemicals.One, two Furthermore, the BCS provides a framework for considering critical factors (dosage, solubility, permeability, and dissolution rate) that may impact a drug's efficacy in the body. Beyond identifying biowaiver-friendly medications, these factors likely also characterize the CQAs that affect in vivo effectiveness. When thinking about quality by design (QbD), it is very important to have a good understanding of these when developing oral pharmaceutical items.3 Because of the heavy regulatory burden on the BCS, the classification scheme rightfully treads carefully when deciding which product properties, such solubility and/or dissolution rate, are most important for limiting oral absorption. Considering that To prioritize patient safety, it is vital to accurately categorize product modifications that cause changes to in vivo performance rather than misclassify those that do not. Permeability is a feature of the drug molecule that is not expected to vary with product and process changes, hence changes to the

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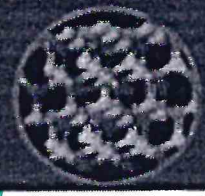

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A randomised, parallel, open-label clinical study comparing the effectiveness and safety of apremilast with methotrexate in individuals with moderate to severe palmoplantar psoriasis.

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GOKULA KRISHNA COLLEGE OF PHARMACY

Abstract:

Various studies have revealed varying outcomes regarding the safety and effectiveness of apremilast in comparison to methotrexate. Therefore, more research into the function of Apremilast in palmoplantar psoriasis is required.Patients with moderate to severe palmoplantar psoriasis were the subjects of a randomized, prospective, parallel-group, open-label trial. For 16 weeks, they were randomly assigned to either the methotrexate group (n = 19) or the apremilast group (n = 22). Reduced scores on the modified palmoplantar psoriasis severity index (mPPPASI) from week 0 to week 16 served as the primary effectiveness metric. Additional metrics included the percentage of patients who achieved a Static Physician Global Assessment score of 0 (clear) or 1 (almost clear), the percentage of patients who achieved mPPPASI75 (75% reduction in mPPPASI score) by the end of 16 weeks, and the proportion of patients who demonstrated a dermatology life quality index decline of at least 5àpoints from the beginning.At 16 weeks, there was no statistically significant difference between the two groups in terms of m-PPPASI score drop, however there was a significant decline from week 0 to week 16 within the group. The secondary efficacy measures had identical outcomes. Out of the twenty-four adverse events documented in the methotrexate group, three individuals had abnormal liver function tests. Out of the 19 adverse events documented in the apremilast group, 2 patients had an infection of the upper respiratory tract.In the treatment of moderate to severe palmoplantar psoriasis, apremilast is just as effective as methotrexate, but it is more tolerable.Static Physician Global Assessment, Dermatology Life Quality Index, Palmoplantar Psoriasis, Palmoplantar Psoriasis Area and Severity Index, Apremilast

It is more likely for psoriasis to appear before the age of 30. The high expense of therapy and the significant psychological and social effects of psoriasis have a negative effect on sufferers' quality of life (QOL).[2]

Scalp, face, intertrigonous, genital, palmoplantar, and nail psoriasis are the many types of psoriasis that may be found. Patients with palmoplantar psoriasis have more limited mobility and fewer self-care options, and they also have varying responses to medicines.the thirdTopical

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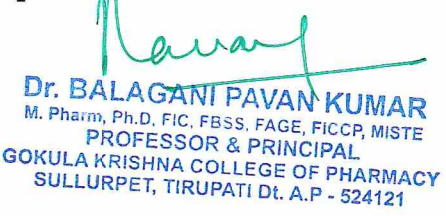

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CALENDER YEAR - 2020

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2	The Proteome of Filter-Grown Caco-2 Cells With a Focus on Proteins Involved in Drug Disposition	Mr.Sivakumar Peta	History of Medicine studies	1300-669
3	The Proteome of Filter-Grown Caco-2 Cells With a Focus on Proteins Involved in Drug Disposition	Mr.S Bugga Reddy	History of Medicine studies	1300-669
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History of Medicine Studies
ISSN:1300-669
Volume 16 Issue 2Aug 2020

The Proteome of Filter-Grown Caco-2 Cells With a Focus on Proteins Involved in Drug Disposition

Ms. C B Hanisha , Mr.Sivakumar Peta ,Mr.S Bugga Reddy , Mr AVLS Ramakrishna , Ms M Sowmya

Abstract

Research on the physiology of intestinal cells and drug transport often makes use of Caco-2 cells. In this study, the total protein technique was used to quantify the global proteome of filter-grown Caco-2 cells. The results were compared with proteomes from the human colon and jejunum. There were a total of 8096 proteins found. Thorough examination of proteins that characterize enterocyte development, such as adherens and tight junctions, integrins, and brush-border hydrolases, provided almost exhaustive coverage of the anticipated proteins. Out of the 327 proteins that were found, 112 were solute carriers and 20 were ATP-binding cassette transporters; these proteins were involved in absorption, distribution, metabolism, and excretion. The levels of OATP2B1 were sixteen times more in Caco-2 cells compared to jejunum. At clinically relevant intestine concentrations, OATP2B1 accounted for 60%-70% of the uptake kinetics of pitavastatin, an OATP2B1 substrate, in Caco-2 monolayers. We aimed to understand how this discrepancy affected in vitro-in vivo extrapolations. Together, pitavastatin kinetics and transporter concentrations were used to simulate the role of active transport and membrane penetration in the jejunum. Pitavastatin absorption in vivo is mostly mediated via transmembrane diffusion, as shown by the much decreased transporter contribution (<5%) caused by the lower OATP2B1 expression in the jejunum. The first comprehensive measurement of the Caco-2 proteome produced in a filter has been presented here. To correctly interpret drug transport pathways in the human gut, we also show that transporter expression levels are very important.

Introduction

The human colon carcinoma Caco-2 cell line was originally iso- lated by Fogh et al.[1] Zweibaum et al. introduced the use of filter- grown Caco-2 monolayers for studies of epithelial cell physiology and reported on its spontaneous differentiation to an enterocyte- like phenotype.[2,3] This paved the way for scientists in the pharma- ceutical field to apply this cell line for the study of solute transport and absorption. [4-7]

Borchardt and Wilson were the first to use Caco-2 cells to study active transport processes, including transport of bile proteins, vitamins, amino acids, and peptides.6,8-10 Since methods for identifying or knocking off the target transporter were just recently developed, functional studies dominated their groundbreaking work and the subsequent many investigations. Modern mass spectrometry has made it feasible to map the whole Caco-2 cell proteome.

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The Proteome of Filter-Grown Caco-2 Cells With a Focus on Proteins Involved in Drug Disposition

Ms. C B Hanisha , Mr.Sivakumar Peta ,Mr.S Bugga Reddy , Mr AVLS Ramakrishna ,
Ms M Sowmya

Abstract

Research on the physiology of intestinal cells and drug transport often makes use of Caco-2 cells. In this study, the total protein technique was used to quantify the global proteome of filter-grown Caco-2 cells. The results were compared with proteomes from the human colon and jejunum. There were a total of 8096 proteins found. Thorough examination of proteins that characterize enterocyte development, such as adherens and tight junctions, integrins, and brush-border hydrolases, provided almost exhaustive coverage of the anticipated proteins. Out of the 327 proteins that were found, 112 were solute carriers and 20 were ATP-binding cassette transporters; these proteins were involved in absorption, distribution, metabolism, and excretion. The levels of OATP2B1 were sixteen times more in Caco-2 cells compared to jejunum. At clinically relevant intestine concentrations, OATP2B1 accounted for 60%-70% of the uptake kinetics of pitavastatin, an OATP2B1 substrate, in Caco-2 monolayers. We aimed to understand how this discrepancy affected in vitro-in vivo extrapolations. Together, pitavastatin kinetics and transporter concentrations were used to simulate the role of active transport and membrane penetration in the jejunum. Pitavastatin absorption in vivo is mostly mediated via transmembrane diffusion, as shown by the much decreased transporter contribution (<5%) caused by the lower OATP2B1 expression in the jejunum. The first comprehensive measurement of the Caco-2 proteome produced in a filter has been presented here. To correctly interpret drug transport pathways in the human gut, we also show that transporter expression levels are very important.

Introduction

The human colon carcinoma Caco-2 cell line was originally iso- lated by Fogh et al.[1] Zweibaum et al. introduced the use of filter- grown Caco-2 monolayers for studies of epithelial cell physiology and reported on its spontaneous differentiation to an enterocyte- like phenotype.[2,3] This paved the way for scientists in the pharma- ceutical field to apply this cell line for the study of solute transport and absorption. [4-7]

Borchardt and Wilson were the first to use Caco-2 cells to study active transport processes, including transport of bile proteins, vitamins, amino acids, and peptides.6,8-10 Since methods for identifying or knocking off the target transporter were just recently developed, functional studies dominated their groundbreaking work and the subsequent many investigations. Modern mass spectrometry has made it feasible to map the whole Caco-2 cell proteome.

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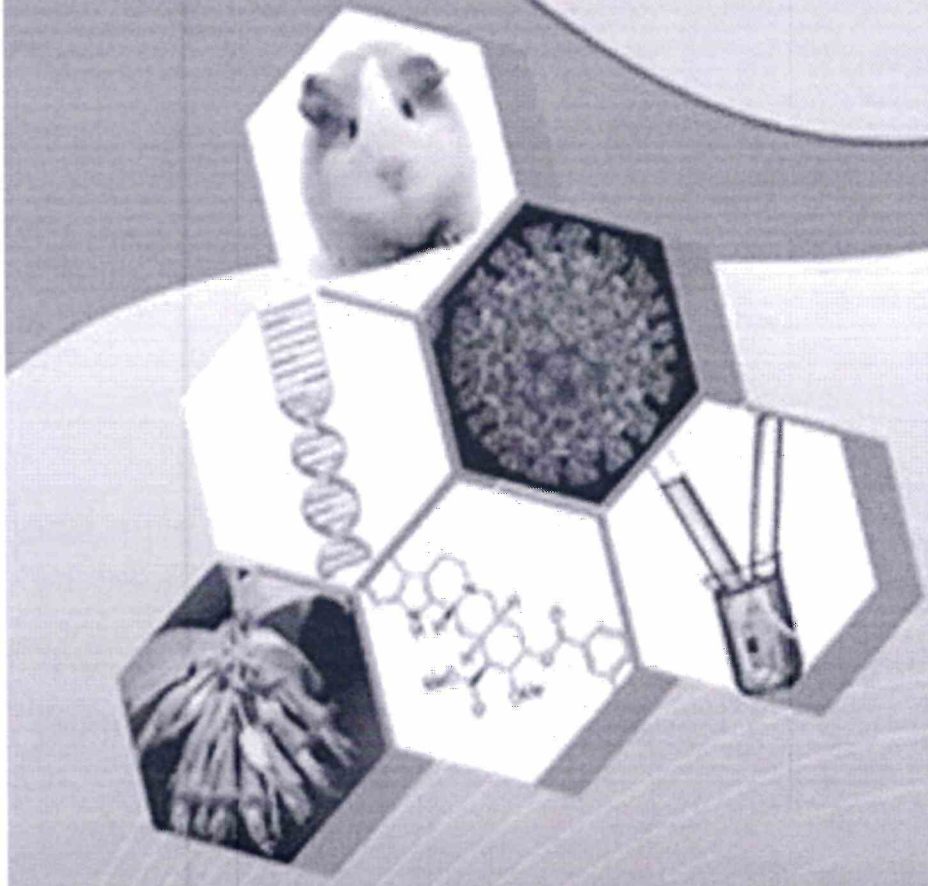

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Keywords: *Factorial Design; Validation; RP-HPLC; ICH guideline; Valethamate bromide (VLB)*

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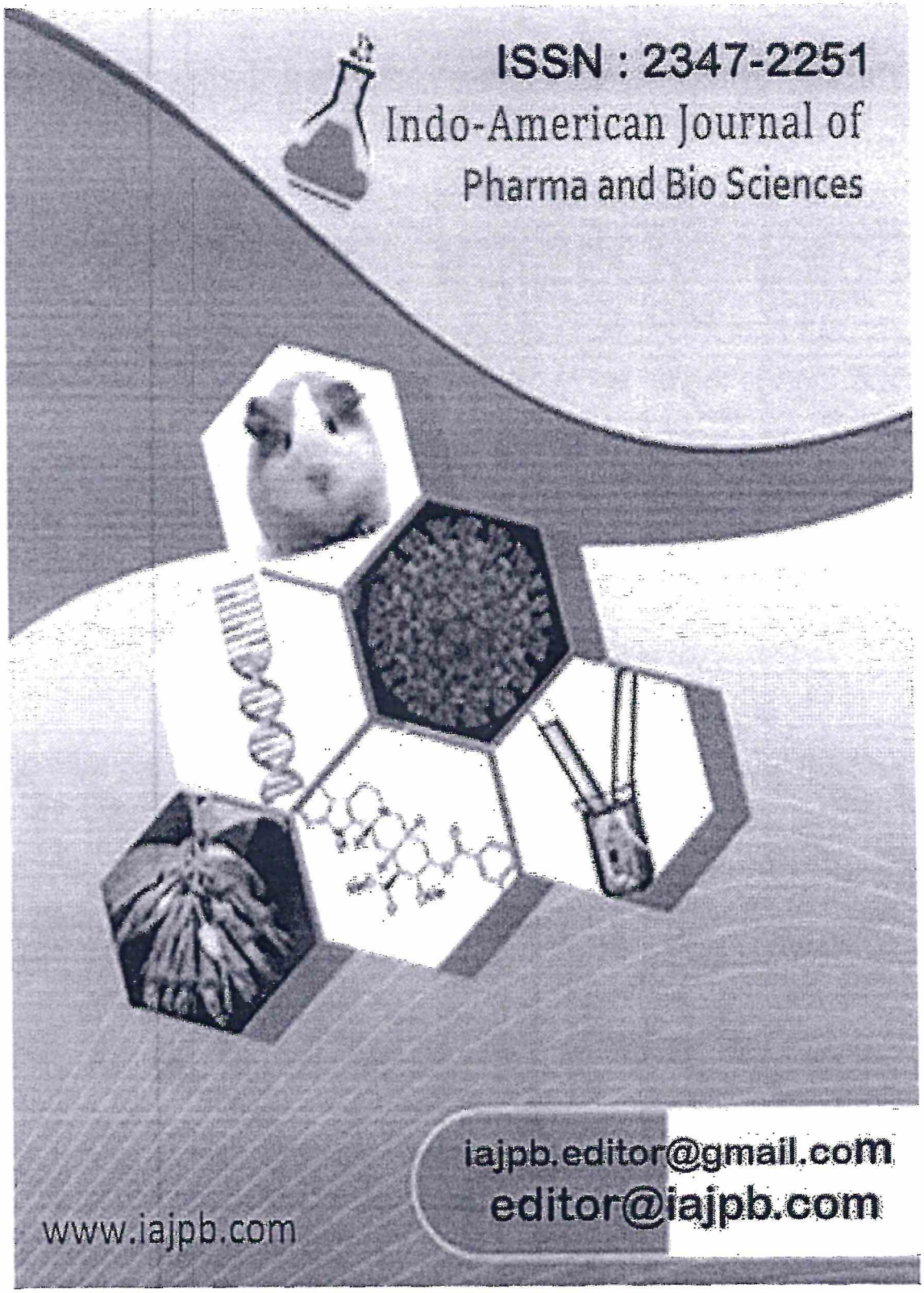

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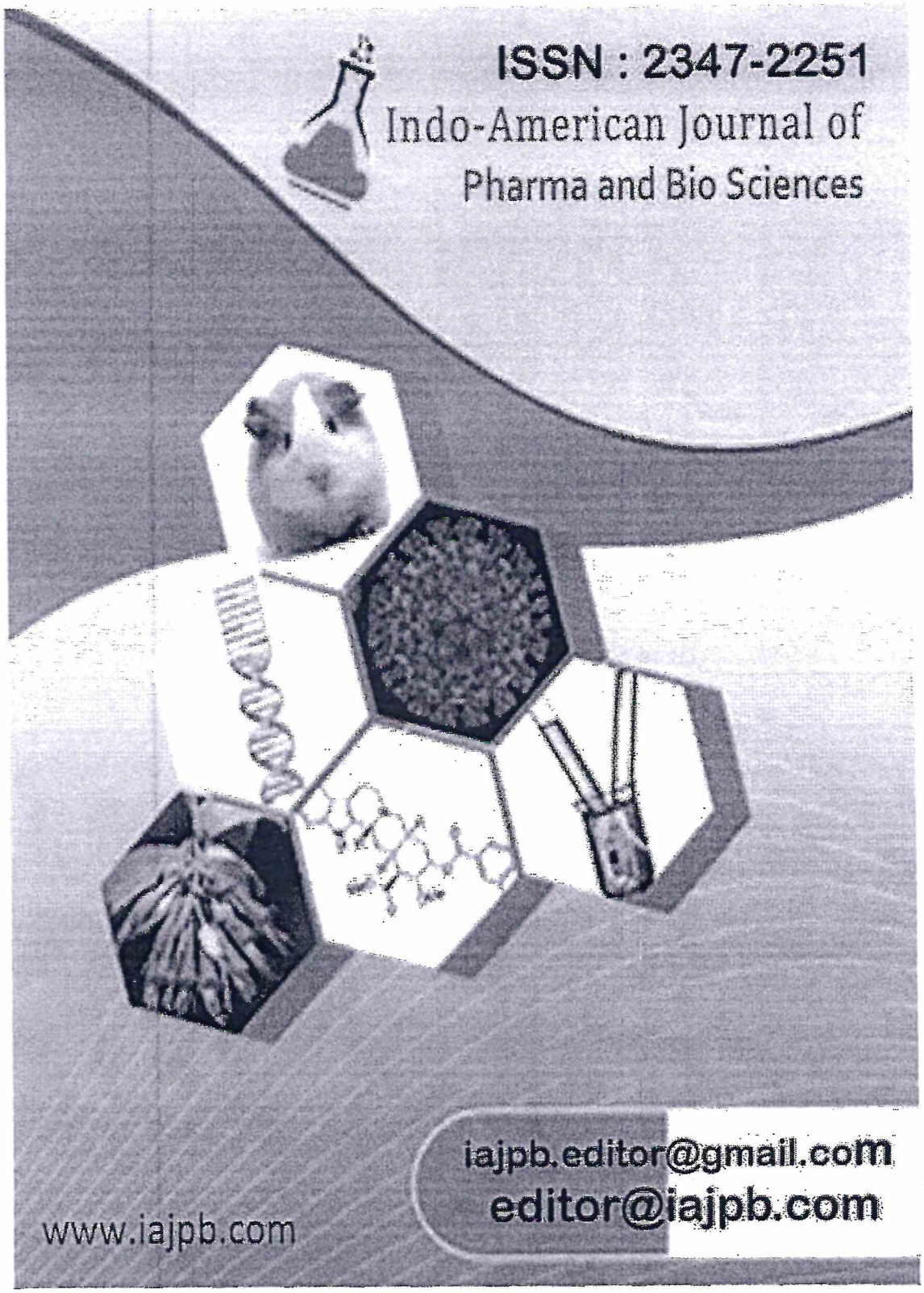

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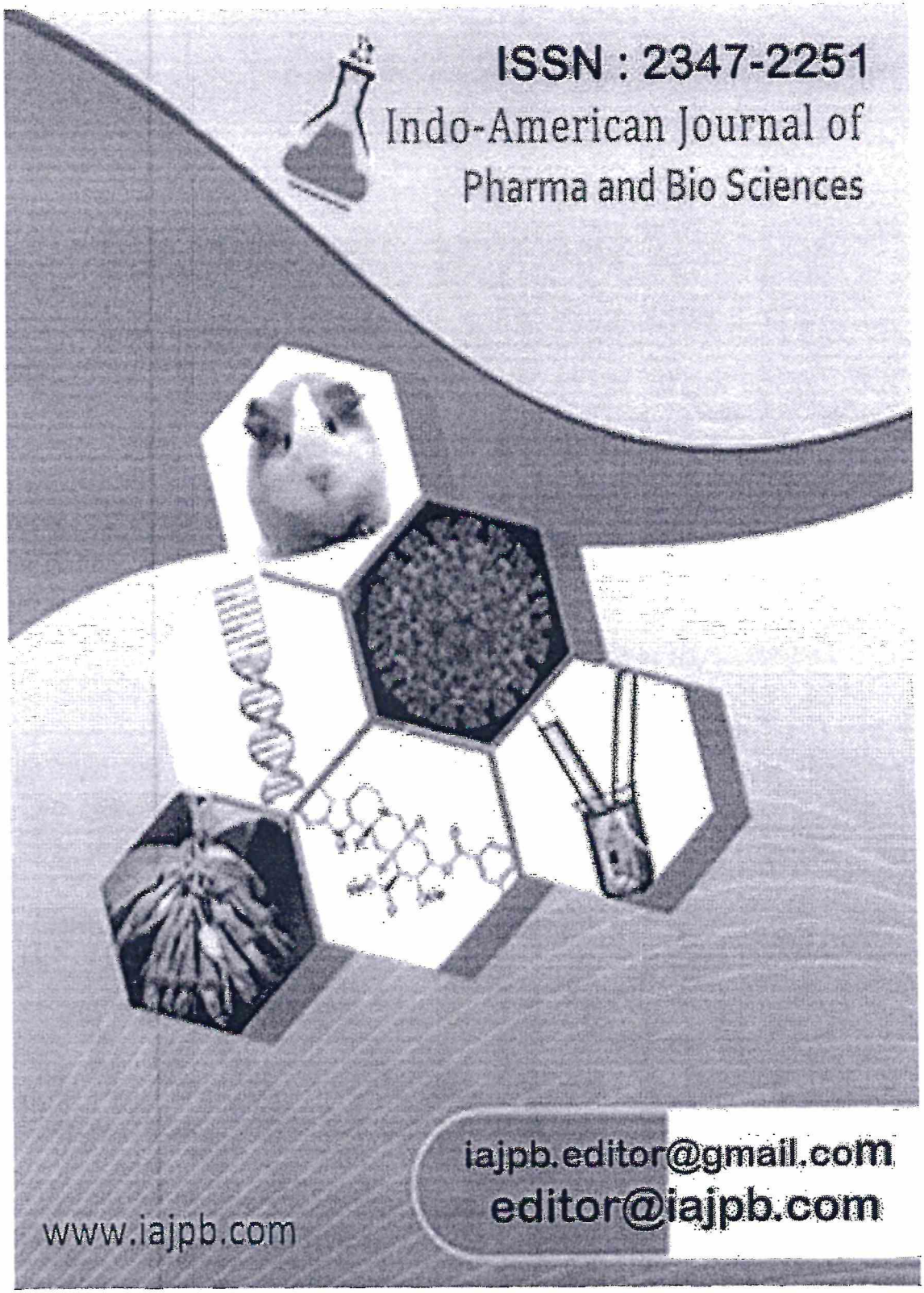

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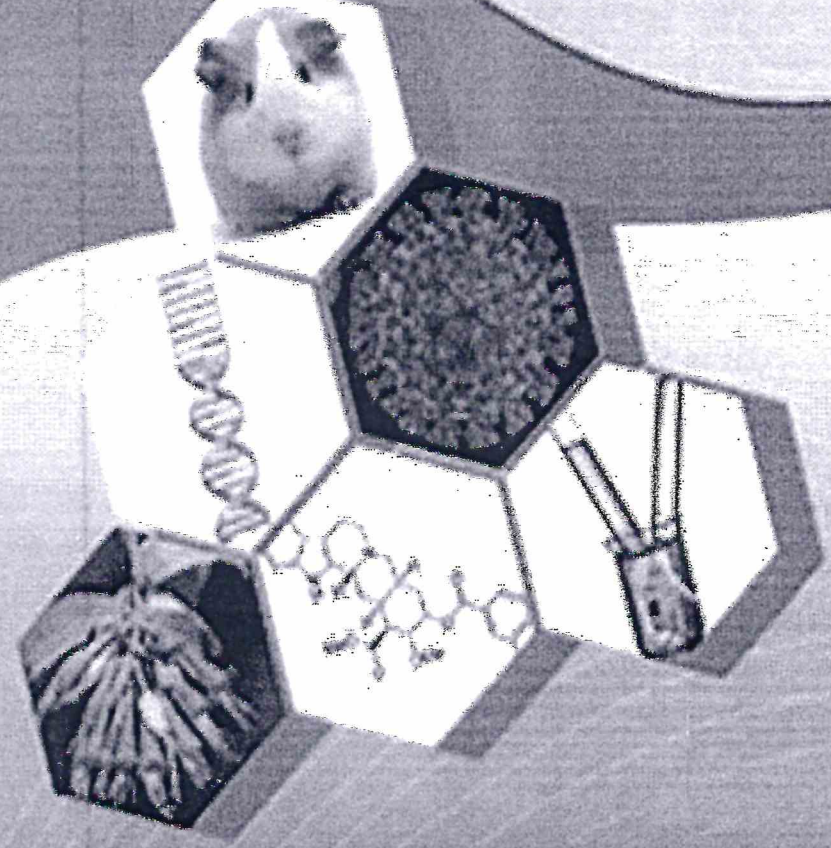

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Ms A R Sridevi *et. al* International Journal of Pharmacetical Sciences Letters

A tertiary care hospital's drug resistance profile in instances of gastrointestinal and postbiliary surgical-site infections

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Abstract:

Surgical-site infection (SSI)-associated bacteria in underdeveloped regions are showing signs of increasing medication resistance, which is leading to more severe complications and increased healthcare expenses. The pattern of medication resistance in our SSI-related isolates was our aim in this analysis. Wound swabs were treated using standard aerobic and anaerobic culture for 191 clinically confirmed SSIs (postbiliary tract and postgastrointestinal surgery) during a 2-year period. The Epsilometer was used to determine the minimum inhibitory concentration (MIC) of the antibiotic. According to the criteria, phenotypes of multidrug resistance were identified. There were 5.3% SSIs, mostly caused by Klebsiella, Staphylococcus, and Pseudomonas, with no anaerobes found. Nineteen percent of the Staphylococcus aureus bacteria were resistant to methicillin, and a third of those bacteria showed an elevated macrolide minimum inhibitory concentration (MIC). Out of all the Enterobacteriaceae isolates, about 58.2% were found to generate extended-spectrum beta-lactamases. We found isolates that had a higher meropenem MIC. The dangerously increasing proportion of antibiotic resistance in SSI patients is accompanied with MICs that are rapidly nearing resistance in susceptible isolates. Immediate remedial measures are required by law.

Search Terms:

Minimum inhibitory concentration, health care-associated infection, surgical-site infection, extended-spectrum beta-lactamase, and methicillin-resistant Staphylococcus aureus Despite being avoidable in over half of instances, surgical-site infections (SSIs) are linked to higher rates of patient morbidity, death, and healthcare-associated costs.Up to 30% of patients in poor and medium income countries who have surgery are affected by surgical site infections (SSIs), making them the most prevalent kind of healthcare-associated illness (HAI).[2] SSI is the second most common kind of healthcare-associated infection (HAI), accounting for up to 20% of all HAIs in developed nations.[5]

Introduction

The average SSI rate here was 4.2%, according to a comprehensive multicentric research that included data from six Indian cities.Bacterial isolates associated with SSIs are typically found in healthcare settings, where medication resistance is prevalent. Drug resistance may be associated with surgery-related variables such emergency operations and extended surgical prophylaxis.For

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Surgical-site infection (SSI)-associated bacteria in underdeveloped regions are showing signs of increasing medication resistance, which is leading to more severe complications and increased healthcare expenses. The pattern of medication resistance in our SSI-related isolates was our aim in this analysis. Wound swabs were treated using standard aerobic and anaerobic culture for 191 clinically confirmed SSIs (postbiliary tract and postgastrointestinal surgery) during a 2-year period. The Epsilometer was used to determine the minimum inhibitory concentration (MIC) of the antibiotic. According to the criteria, phenotypes of multidrug resistance were identified. There were 5.3% SSIs, mostly caused by Klebsiella, Staphylococcus, and Pseudomonas, with no anaerobes found. Nineteen percent of the Staphylococcus aureus bacteria were resistant to methicillin, and a third of those bacteria showed an elevated macrolide minimum inhibitory concentration (MIC). Out of all the Enterobacteriaceae isolates, about 58.2% were found to generate extended-spectrum beta-lactamases. We found isolates that had a higher meropenem MIC. The dangerously increasing proportion of antibiotic resistance in SSI patients is accompanied with MICs that are rapidly nearing resistance in susceptible isolates. Immediate remedial measures are required by law.

Search Terms:

Minimum inhibitory concentration, health care-associated infection, surgical-site infection, extended-spectrum beta-lactamase, and methicillin-resistant Staphylococcus aureus Despite being avoidable in over half of instances, surgical-site infections (SSIs) are linked to higher rates of patient morbidity, death, and healthcare-associated costs.Up to 30% of patients in poor and medium income countries who have surgery are affected by surgical site infections (SSIs), making them the most prevalent kind of healthcare-associated illness (HAI).[2] SSI is the second most common kind of healthcare-associated infection (HAI), accounting for up to 20% of all HAIs in developed nations.[5]

Introduction

The average SSI rate here was 4.2%, according to a comprehensive multicentric research that included data from six Indian cities.Bacterial isolates associated with SSIs are typically found in healthcare settings, where medication resistance is prevalent. Drug resistance may be associated with surgery-related variables such emergency operations and extended surgical prophylaxis.For

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Ms A R Sridevi *et. al* International Journal of Pharmacetical Sciences Letters

A tertiary care hospital's drug resistance profile in instances of gastrointestinal and postbiliary surgical-site infections

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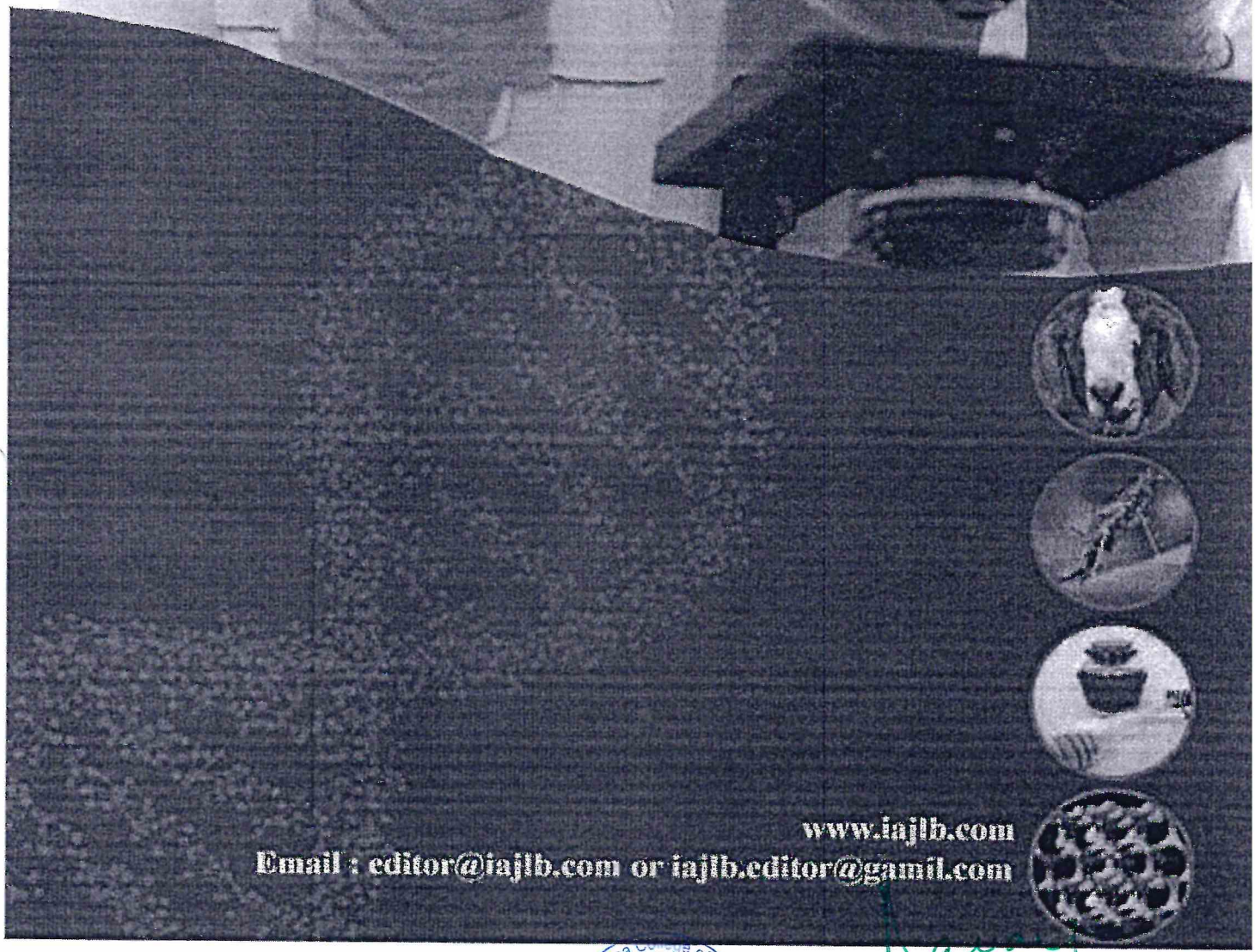

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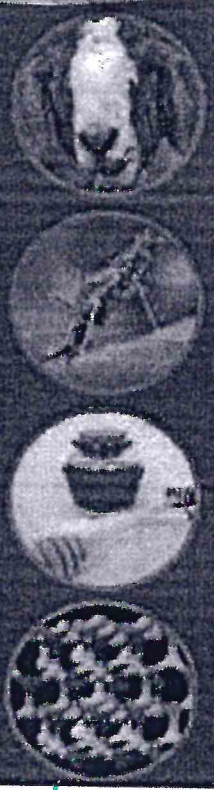

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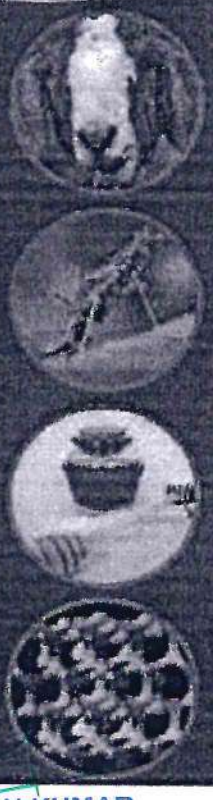

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3	3-Thiocyanato- 1*H*- indoles as potential anticancer agents: Two dimensional quantitative structure activity relationship study	Mrs.S.Usharani	International Journal of Pharmaceutical Sciences Letters	2277-2685
4	3-Thiocyanato- 1*H*- indoles as potential anticancer agents: Two dimensional quantitative structure activity relationship study	Mr.B.Kondalrao	International Journal of Pharmaceutical Sciences Letters	2277-2685
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3-Thiocyanato- 1*H*- indoles as potential anticancer agents: Two dimensional quantitative structure activity relationship study

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Analysis on fat-soluble components of sinapis seminafrom different habitats by GC–MS

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KEYWORDS : Sinapis semina, GC/MS, fingerprinting, and hydrophilic extraction

1. Introduction

Dried Sinapis semina are the seeds of the Sinapis alba lineage. Among the pharmacological effects of this traditional Chinese medicine include anti-cancer, analgesic, and antiviral properties [1]. Sapidus semina relies on its fat-soluble components. Isolating and identifying the fat-soluble chemicals is crucial for sinapis semina study. Gas chromatography/mass spectrometry (GC-MS) and gas chromatography have seen extensive application for the investigation of herbal medicines' fat-soluble components [2,3]. As an especially applicable and trustworthy technique, GC/MS has been used for the determination of plant medicinal components that are fat-soluble, because of their superior capacity for isolation and identification.

To ensure the efficacy of herbal medicines, quality control is essential, and one aspect of this procedure is regularly monitoring the amounts of chemical ingredients [4,5]. Herbal remedies have a complicated chemical makeup, and the quantification of substances depends on factors such as harvest time, storage conditions, processing technique, and environmental factors. A lot of places have started growing Sinapis semina.

country. Sinapis semina's impact is associated with its fat-soluble components, which come from several places.

Quantitative extraction of fat-soluble components from herbal medicines has been accomplished using a variety of procedures, such as steam distillation, solvent immersion, and solid-phase extraction [6, 7, 8]. Having said that, these approaches are tedious and time consuming. The fast extraction of herbal medicine's fat-soluble components has been achieved by the use of sonication extraction. Its low organic solvent consumption and ease of operation make it a practical choice [9–12].

It is not sufficient to only quantify one or even many substances in herbal medicine in order to assess the quality of sinapis semina. One form of thorough, quantifiable chromatographic identification approach is the Chinese medicine chromatographic fingerprint technique. A comprehensive analysis of the chemical composition of Chinese herbal medicine forms the basis of the technique. There has been a recent uptick in interest in chromatographic fingerprint analysis of herbal medicines [13–16]. This is because the technology incorporates the holistic and systemic aspects of Chinese traditional medicine. In addition, by comparing how similar two samples are,

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The fat-soluble components of sinapis semina were identified using a fast and easy gas chromatography/mass spectrometry (GC/MS) analytical technique. In order to test the efficacy of the procedure, four chemicals were selected as marker compounds. Following an analysis of many extraction methods, sonication extraction with diethyl ether proved to be the most effective. After checking the resolutions, tailing factors, and theoretical plate number of the marker chemicals, we were able to determine that the apparatus was suitable for the approach. We also checked that the accuracy and repeatability, measured as relative standard deviation (RSD), were within the allowed limits. Eight sinapis semina samples were tracked using the approach after being acquired from Xi'an markets. Hierarchical cluster analysis (HCA) similarity analysis was used to examine the fingerprints of those samples. A combination of fingerprint and HCA allowed for the analysis of sinapis semina from various habitats, according to the results.

KEYWORDS : Sinapis semina, GC/MS, fingerprinting, and hydrophilic extraction

1. Introduction

Dried Sinapis semina are the seeds of the Sinapis alba lineage. Among the pharmacological effects of this traditional Chinese medicine include anti-cancer, analgesic, and antiviral properties [1]. Sapidus semina relies on its fat-soluble components. Isolating and identifying the fat-soluble chemicals is crucial for sinapis semina study. Gas chromatography/mass spectrometry (GC-MS) and gas chromatography have seen extensive application for the investigation of herbal medicines' fat-soluble components [2,3]. As an especially applicable and trustworthy technique, GC/MS has been used for the determination of plant medicinal components that are fat-soluble, because of their superior capacity for isolation and identification.

To ensure the efficacy of herbal medicines, quality control is essential, and one aspect of this procedure is regularly monitoring the amounts of chemical ingredients [4,5]. Herbal remedies have a complicated chemical makeup, and the quantification of substances depends on factors such as harvest time, storage conditions, processing technique, and environmental factors. A lot of places have started growing Sinapis semina.

country. Sinapis semina's impact is associated with its fat-soluble components, which come from several places.

Quantitative extraction of fat-soluble components from herbal medicines has been accomplished using a variety of procedures, such as steam distillation, solvent immersion, and solid-phase extraction [6, 7, 8]. Having said that, these approaches are tedious and time consuming. The fast extraction of herbal medicine's fat-soluble components has been achieved by the use of sonication extraction. Its low organic solvent consumption and ease of operation make it a practical choice [9–12].

It is not sufficient to only quantify one or even many substances in herbal medicine in order to assess the quality of sinapis semina. One form of thorough, quantifiable chromatographic identification approach is the Chinese medicine chromatographic fingerprint technique. A comprehensive analysis of the chemical composition of Chinese herbal medicine forms the basis of the technique. There has been a recent uptick in interest in chromatographic fingerprint analysis of herbal medicines [13–16]. This is because the technology incorporates the holistic and systemic aspects of Chinese traditional medicine. In addition, by comparing how similar two samples are,

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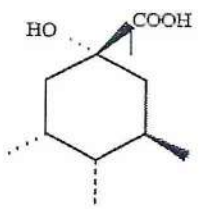

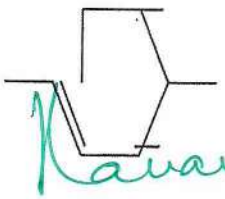

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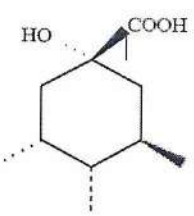

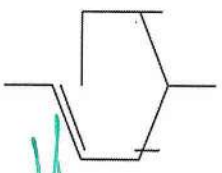

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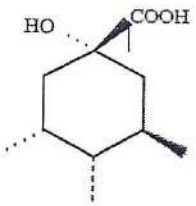

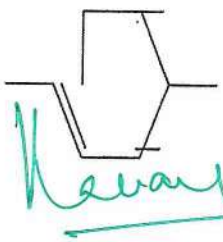

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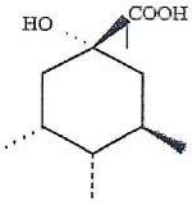

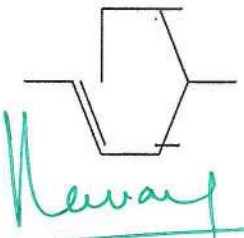

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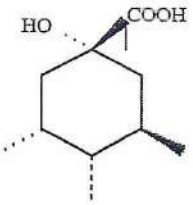

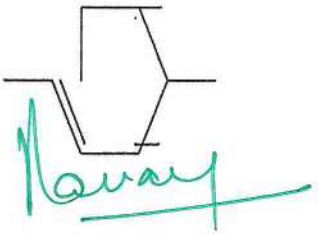

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A Study on the Characterization and Stability Implications of Investigating Local Mobility in Amorphous Pharmaceuticals

Mrs. P K Devibala,Dr.B. Pavan kumar , Ms KVanithadevi ,MR B Kondalrao , Mrs Y Swaroopa

ABSTRACT: There has been a deluge of research on the relationship between molecular mobility and the physical and chemical stability of amorphous drugs in recent years. Glass transition and global mobility-related molecular movements have been the primary targets of these investigations. There were, however, a handful of cases where the volatility could not be explained by international migration. The idea that b-relaxations, which occur at local scales well below the glass transition temperature, may be impacting stability is gaining traction. One common method for determining an amorphous pharmaceutical's mobility below the glass transition temperature (Tg) is to extrapolate data collected above Tg. While not well-suited to pinpointing precise local mobility, this kind of investigation may provide data about mobility in general. Our main goal from a pharmacological standpoint is to prove that local movements are important in amorphous drugs, especially in the Johari-Goldstein relaxations. In order to highlight the possible influence of local mobility on the stability of amorphous phases, an assessment of the coupling model was carried out that linked local movements with global mobility. We took into account the effects of water and other additives when studying the local movements in an amorphous matrix present in molecular dispersions. In conclusion, we have offered a concise review, highlighting the advantages and disadvantages, of the most widely used instrumental methods for characterizing local movements. To this day, Wiley-Liss, Inc., the publisher, has all rights.

Keywords: Amorphous, solid dispersion, lyophilization, mobility, and crystallization

INTRODUCTION

Pharmaceutical companies often produce amorphous forms of certain APIs used in drug formulation.1 An increasingly well-known problem that this method solves is the sluggish pace of dissolution caused by compounds' poor water solubility.1 As a result of their higher free energies, amorphous states may be less physically stable; crystallization tendencies are one indicator of this. Reduced chemical stability may also cause an intolerably short storage life. Thus, there is a lot of focus in the field right now on predicting stability and making amorphous pharmaceuticals. Investigators in the pharmaceutical industry have good cause to wonder if there is a link between molecular dynamics and the stability of amorphous phases.

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Keywords: Amorphous, solid dispersion, lyophilization, mobility, and crystallization

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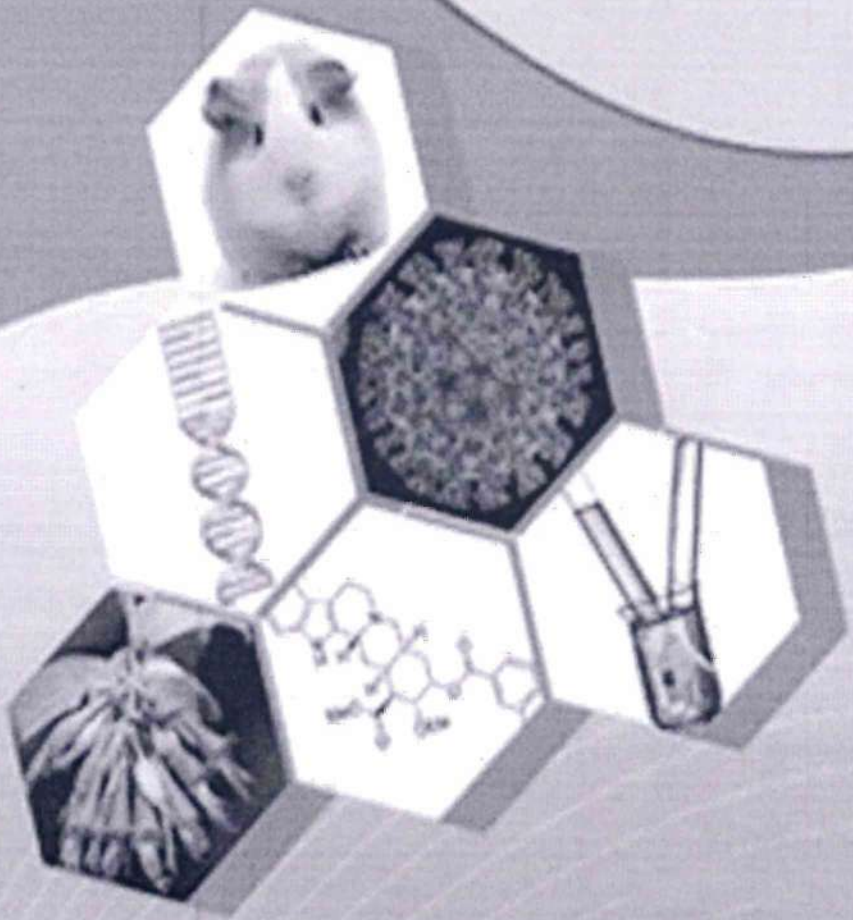

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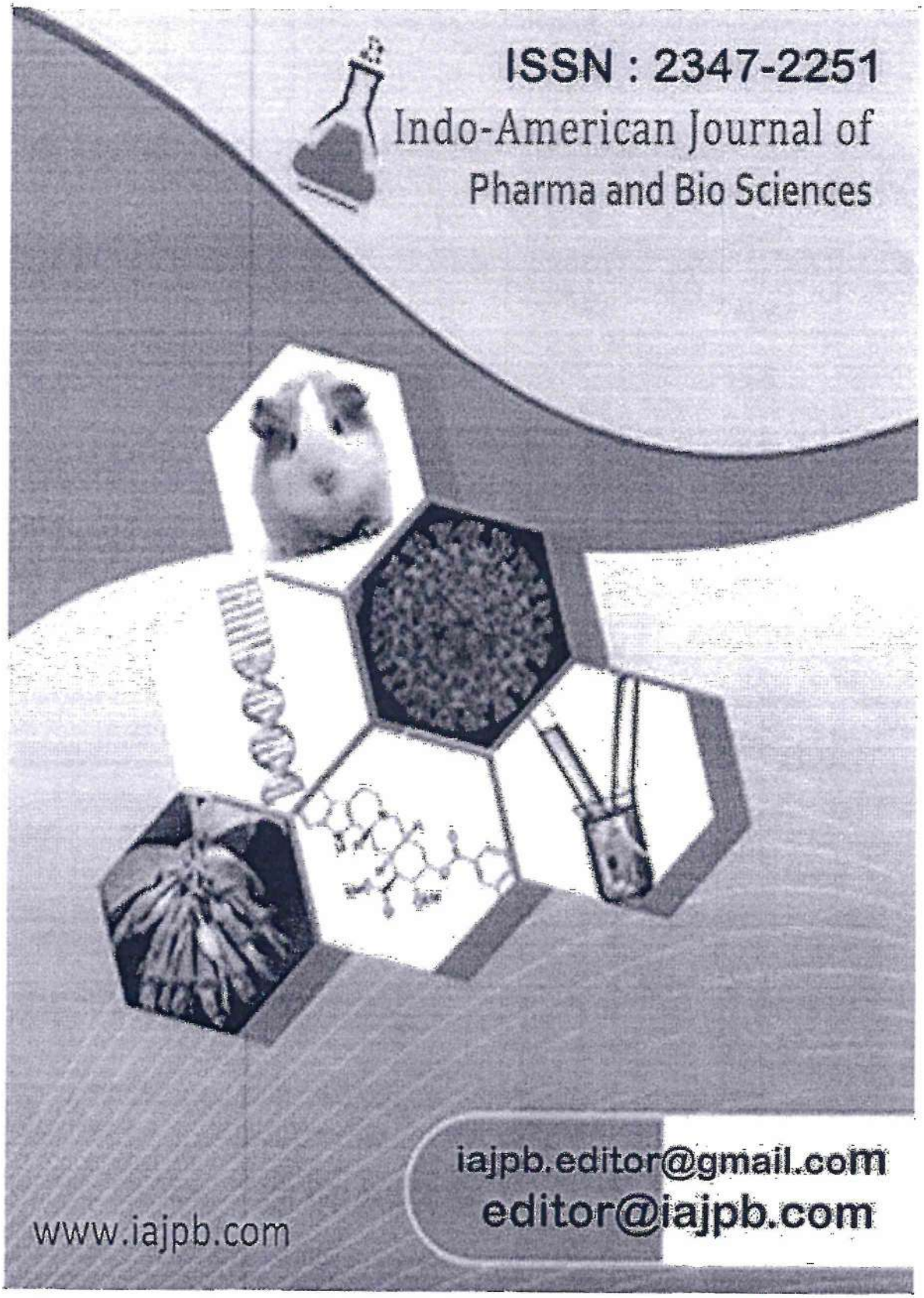

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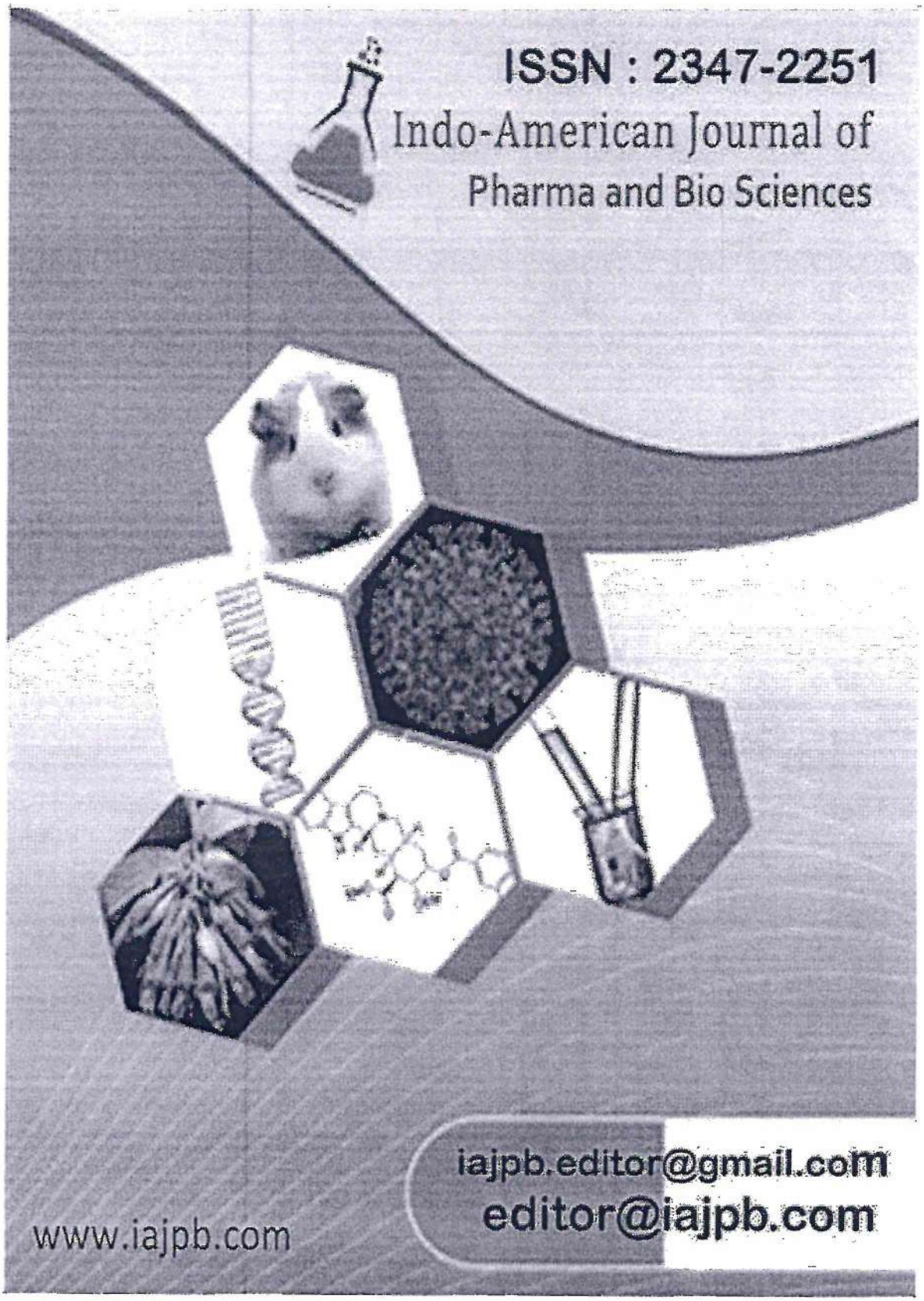

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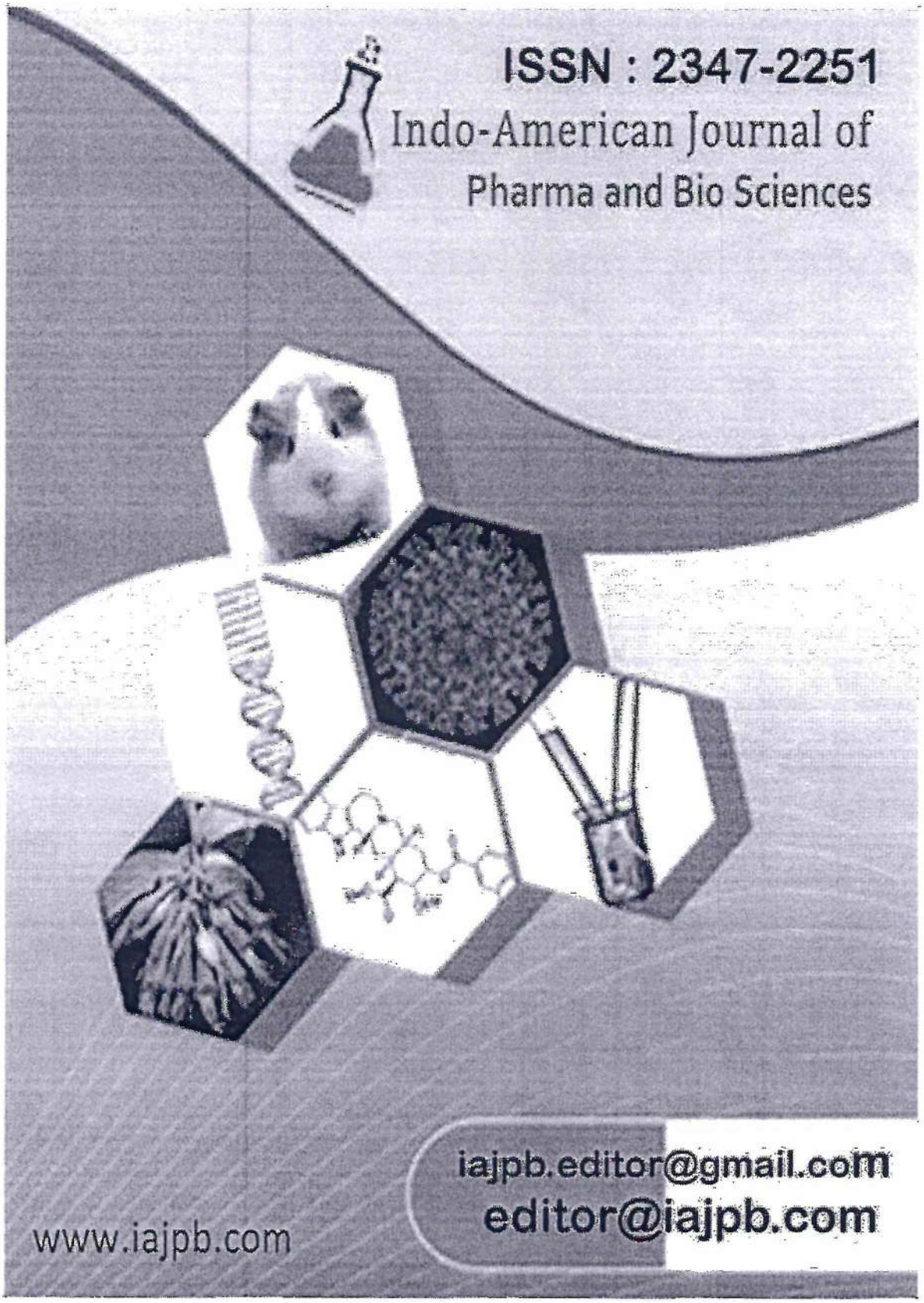

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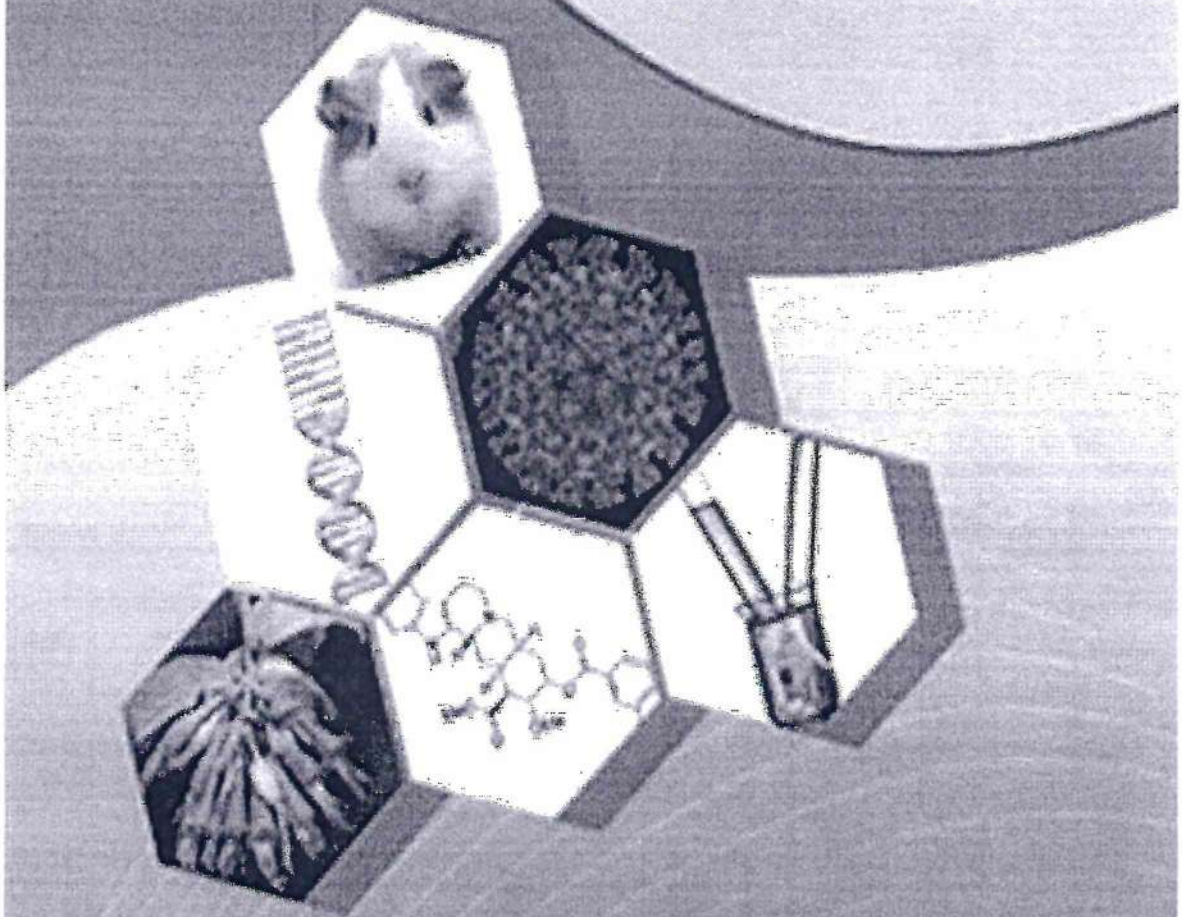

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The oral cavity is of great importance to the performance of orally retained formulations, including: ora disintegrating tablets, taste-masked formulations, and buccal/sublingual delivery systems. With regards to *in vi* dissolution assessment of these dosage forms, human saliva should be represented by the dissolution med Currently there is no general consensus regarding oral cavity dissolution. In this study pooled human saliva w characterised and utilised as dissolution media for biorelevant oral cavity dissolution studies and to assess dr release. Lipophilic drug felodipine with challenging biopharmaceutical properties was selected for assessment in o cavity dissolution studies. These saliva dissolution studies investigated for the first time how biorelevant dissoluti can be implemented as a screening tool to guide the formulation development process and to predict dosage for performance within the mouth. In this study a combination of three dissolution enhancement strategies (cryomillir solid dispersion, and inclusion complexation) were employed to eventually increase the concentration of felodipine saliva 150-fold. Using this successful formulation strategy orally disintegrating tablets of felodipine were produce Interestingly, the percentage release of felodipine in compendial dissolution apparatus was shown to be over 80 after 10 min. On the other hand, saliva-based dissolution showed that percentage release of felodipine was on 0.2% after 10 min using the same formulation. This discrepancy in drug release between dissolution med highlights the need for biorelevant dissolution apparatus for the oral cavity to reliably assess performance relevant dosage forms *in vitro*.

1. Introduction

The oral cavity is a site for drug dissolution that is generally over- looked in pharmaceutical development. Following the oral adminis- tration of drugs there are several processes which take place over a relatively short period of time. These processes include: disintegration, dissolution, taste perception, drug absorption, and drug removal via swallowing. Compared to conventional solid oral dosage forms, such as tablets and capsules, orally retain formulations can be greatly im- pacted by the ti spent within the oral cavity. The performance of ora retained formulations such as sublingual and buc tablets, or- ally disintegrating tablets (ODTs), and o films in the oral cavity rely on disintegration a dissolution in saliva (Bartlett and van der Voo Maarschalk, 2012).

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CALENDER YEAR - 2018

S.No	Title of the Paper	Name of the Author/s	Name of the Journal	ISSN NO
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2	A thorough analysis of Thymus serpyllum's traditional uses, phytochemistry, pharmacology, and toxicity	Ms.B.Geethanjali Bai.	International Journal of Pharmaceutical Sciences Letters	2277-2685
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Ms.A R Sridevi *et. al* International Journal of Pharmacetical Sciences Letters

A thorough analysis of Thymus serpyllum's traditional uses, phytochemistry, pharmacology, and toxicity

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Keywords:

Pharmacological properties, phytochemistry, *Thymus serpyllum*, toxicity, traditional applications

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The contemporary world is responsible for improving immune responses and achieving excellent health via the use of medicinal herbs. For generations, from 4000 to 5000 B.C., people have turned to traditional remedies as a cost-effective and easily accessible means of illness treatment. The first known medicinal formulation derived from herbs was acquired by the Chinese. The first text on the use of plants as medicines in India was found in the Rig-Veda, which dates back to 1600-3500 B.C. Traditional Indian medicine has long made use of herbs for their therapeutic properties.[1] New medicinal treatments may be derived from plants.

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Indo-American Journal of Life Sciences and Biotechnology

A four-strain probiotic exerts positive immunomodulatory effects by enhancing colonic butyrate production in vitro

Ms.P Kavitha ,Mr.K.R.S.C Bharath kumar,Mrs.M.Sindhuri ,Ms P Madhavi , Mr.Y.Naveenkumar

ABSTRACT - The purpose of this contribution is to evaluate the cytotoxicity and apoptosis inducing ability of structurally diverse anthraquinones to establish a relationship between structure and toxicity. Besides the wide spread use of anthraquinones in pharmacological drugs for constipation and non-prescription dietary supplements for weight loss, extracts are still commercialized as crude extracts and long-term side effects are still relevant. In this work we developed a method to quantify the cascarosides isolated from *Rhamnus purshiana* (Cascara Sagrada) using LC-MS/MS and evaluated the effects of this extract and isolated compounds on cellular viability using NOK-SI, HeLa, and T98G cell lineages. Apoptosis inducing ability was also analyzed via evaluating key-proteins involved in apoptosis pathways. Using cascarosides isolated from bark extracts, we found that the presence of glucose moieties in the chemical structure reduced the toxicity. This communication reviewed the mechanisms of action, toxicity of anthraquinones and correlated the toxicity with chemical structures of cascarosides. Results indicate that cascarosides-enriched cascara extract, as well as glycosylated anthraquinones, may have some beneficial effects for laxative action of herbal medicines. Considering our results, a cascarosides-enrichment in cascara extract is recommended.

INTRODUCTION

Anthraquinones are extensively present in nature, found in plants, bacteria, fungi, and insects. They are widely used as pharmacological drugs for constipation and as non-prescription dietary supplements for weight loss. Currently, these compounds are used to treat a variety of conditions because of their wide ranging biological activities, including anti-inflammatory, antifungal, antibacterial, antiviral, and antiarthritic actions (1).

Due to the cytotoxic action of some anthraquinone components, as doxorubicin (natural), daunorubicin (natural) and valrubicin (semisynthetic), several medicines have been developed to treat cancer (1-3). One important mechanism of action for cytotoxic agents used in cancer treatment is apoptosis induction. However, apoptosis is also responsible for the long-term sideeffects – as mucosa darkening – of anthraquinone- rich plants.

The mucosa darkening, also known as pseudo- melanosis coli, is a lipofuscin-like pigment found in macrophages from colonic lamina propria. The melanosis coli has been linked to the chronic use of laxative/purgative anthranoid-rich plants (4, 5). Despite effective laxative action of anthraquinone- rich plants, clinical studies demonstrated that 73.4% of patients who chronically used anthranoids laxatives had melanosis coli, showing a clear association between anthraquinones and colon darkening (6). Histological studies have shown that a large number of apoptotic bodies are not caused by natural renewal, but by laxative action, suggesting that melanic substances are formed by the action of anthraquinones (7). Chen *et al.* (8) proposed a melanosis-forming mechanism that correlated the accumulation of pigments to the long-term use of these natural compounds. When such compounds enter the colon, they produce a laxative effect and damage the epithelial cells. These cells release TNF- α for the cell renewal induction mechanism via triggering apoptosis. Furthermore, damaged epithelial cells are phagocytized by macrophages, which migrate to *lamina propria* of the epithelium. In the *lamina propria*, the apoptotic bodies become lipofuscin, giving rise to black patches that darken the colon.

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INTRODUCTION

Anthraquinones are extensively present in nature, found in plants, bacteria, fungi, and insects.They are widely used as pharmacological drugs for constipation and as non-prescription dietary supplements for weight loss. Currently, these compounds are used to treat a variety of conditions because of their wide ranging biological activities, including anti-inflammatory, antifungal, antibacterial, antiviral, and antiarthritic actions (1).

Due to the cytotoxic action of some anthraquinone components, as doxorubicin (natural), daunorubicin (natural) and valrubicin (semisynthetic), several medicines have been developed to treat cancer (1-3). One important mechanism of action for cytotoxic agents used in cancer treatment is apoptosis induction. However, apoptosis is also responsible for the long-term sideeffects – as mucosa darkening – of anthraquinone- rich plants.

The mucosa darkening, also known as pseudo- melanosis coli, is a lipofuscin-like pigment found in macrophages from colonic lamina propria. The melanosis coli has been linked to the chronic use of laxative/purgative anthranoid-rich plants (4, 5). Despite effective laxative action of anthraquinone- rich plants, clinical studies demonstrated that 73.4% of patients who chronically used anthranoids laxatives had melanosis coli, showing a clear association between anthraquinones and colon darkening (6). Histological studies have shown that a large number of apoptotic bodies are not caused by natural renewal, but by laxative action, suggesting that melanic substances are formed by the action of anthraquinones (7). Chen *et al.* (8) proposed a melanosis-forming mechanism that correlated the accumulation of pigments to the long-term use of these natural compounds. When such compounds enter the colon, they produce a laxative effect and damage the epithelial cells. These cells release TNF- α for the cell renewal induction mechanism via triggering apoptosis. Furthermore, damaged epithelial cells are phagocytized by macrophages, which migrate to *lamina propria* of the epithelium. In the *lamina propria*, the apoptotic bodies become lipofuscin, giving rise to black patches that darken the colon.

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INTRODUCTION

The areas of pharmacokinetics and pharmacodynamics (PK/PD) emerged from a long history of understanding basic pharmacological principles, mostly in relation to static or in vitro methods. A wide variety of small-to-large systems models have evolved to capture drug actions at various levels of biological structure, and several basic PK/PD models for in vivo drug effects have evolved into more complicated ones. This review will go over the various areas that have embraced pharmacometrics and PK/PD, highlight key aspects of popular PK/PD models, demonstrate how to construct models that enhance PK/PD and small systems models, and highlight the difficulties in creating more accurate quantitative approaches for larger systems models.

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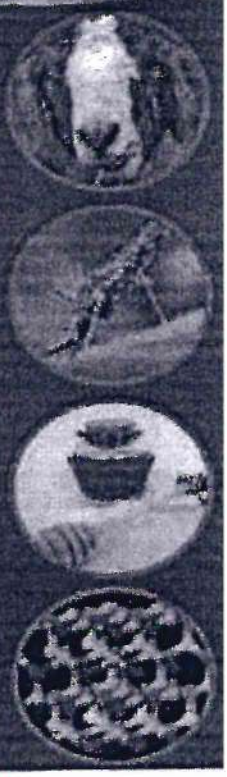

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