CRITERION 3: RESEARCH, INNOVATIONS AND EXTENSION

3.3 – RESEARCH PUBLICATION AND AWARDS

Metric 3.3.1 **Number of research papers published per teacher in the Journals notified on UGC care list during the last five years**

DVV QUERY

1. Publications in the current UGC care with ISSN will only be considered.
2. Calender year publications to be considered (Jan-Dec)

DVV suggested input: 22

Year	2021-22	2020-21	2019-20	2018-19	2017-18
Number	04	07	06	03	02

DVV CLARIFICATION

1. Publications in the current UGC care with ISSN has been considered.
2. Calendar year publications to be considered (Jan-Dec)

DVV suggested input: 20

Year	2021-22	2020-21	2019-20	2018-19	2017-18
Number	04	06	07	01	02

YEARWISE DETAILS

Year	2021-22	2020-21	2019-20	2018-19	2017-18
Number	04	06	07	01	02

Responses: 20

Index

Sr. No.	Title for Research Paper Published	Link
	2021	
1.	In vitro antioxidant potential and anticancer activity of Ceratophyllum demersum Linn. extracts on HT-29 human colon cancer cell line	Link
2.	Anticancer activity of terpenoid saponin extract of Psidium guajava on MCF-7 cancer cell line using DAPI and MTT assays	Link
3.	Chemopreventive potential of adrenergic blocker in behavioral stress accelerated prostate cancer development in rats	Link
4.	Microwave assisted extraction of berberine and preparation of Berberine Hydrochloride from Berberis Aristata Variety of Nepal, and Quantification using RP-HPLC and HPTLC Methods	Link
	2020	
5.	In vitro Antioxidant Potential and Cytotoxicity Study of Asparagus aethiopicus L. Extracts on HT-29 Human Colon Cancer Cell Line	Link
6.	Polymeric nanosuspension loaded oral thin films of flubiprofen: design development and in vitro evaluation	Link
7.	Synthesis of Asymmetric Thiazolyl Pyrazolines as a Potential Antioxidant and Anti-Inflammatory Agents	Link
8.	Design and Evaluation of Eudragit RS-100 Based Itraconazole Nanosuspension for Ophthalmic Application	Link
9.	Eudragit RL100 Based Moxifloxacin Hydrochloride and Ketorolac Tromethamine Combination Nanoparticulate System for Ocular Drug Delivery.PharmaceuticalNanotechnology	Link
10.	Assessment Of Permeability Behavior Of Berberine Chloride Across Goat Intestinal Membrane In Presence Of Natural Biopotentiator Curcumin	Link
	2019	
11.	Formulation and optimization and invitro evaluation of polymeric nano suspension of Fluribiprofen	Link
12.	Design, development and characterization of ketorolac tromethamine Nanosuspension loaded insitu mucoadhesive occular gel	Link

13.	Design and evaluation of topical solid dispersion composite of voriconazole for the treatment of ocular keratitis	Link
14.	Nanostructure lipid carriers (NLC) system: A Novel drug targeting carrier	Link
15.	Optimization of ex vivo permeability characteristics of berberine in presence of Quercetin using 32 full factorial design	Link
16.	POCl3 Mediated Syntheses, Pharmacological Evaluation and Molecular Docking Studies of Some Novel Benzofused Thiazole Derivatives as a Potential Antioxidant and Anti-inflammatory Agents	Link
17.	Evaluation And Comparison Of Antidepressant Activity Of Marketed Ayurvedic Formulations	Link
	2018	
18.	Production and quantitative analysis of Trehalose lipid biosurfactants using HPLC	Link
	2017	
19.	Studies on emulsification properties of glycolipids biosurfactants	Link
20.	Formulation of mild natural biodegradable mycrobeads face scrubber	Link

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RJPT

RESEARCH ARTICLE

In vitro antioxidant potential and anticancer activity of *Ceratophyllum demersum* Linn. extracts on HT-29 human colon cancer cell line

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ABSTRACT:
Objective: To decide the phytochemical constituents, antioxidant and anticancer potential of *Ceratophyllum demersum* Linn. extracts on HT-29 human colon malignant growth cell line. **Methods:** The whole plant was exposed to Hot Soxhlet continuous extraction with expanding polarity of solvents viz., pet ether, chloroform, ethanol, and aqueous maceration. Phytochemical screening was finished utilizing distinctive phytochemical tests. The antioxidant potential was tried utilizing 2, 2-diphenyl-1-picrylhydrazyl, ferric ion reducing power assay and phosphomolybdenum assay. In vitro anticancer action tried on HT-29 human colon malignant growth cell line and it was assessed by (3-(4, 5-dimethyl thiazole-2yl)- 2, 5-diphenyl tetrazolium bromide) MTT test. **Results and Discussion:** Preliminary Phytochemical screening affirmed the presence of phytoconstituents like alkaloids, flavonoids, glycosides, saponins, sterols, tannins, and reducing sugar. Antioxidant potential was demonstrated most noteworthy in ethanol extracts dependent on the test performed. The ethanol extracts were seen as specifically cytotoxic to HT-29 human colon malignant growth cell line. **Conclusion:** The outcomes show that *Ceratophyllum demersum* Linn. was a promising antioxidant; and anticancer agent for HT-29 human colon malignancy cell line. In any case, further examinations are expected to presume that the particular constituent liable for its antioxidant action and cancer prevention agent.

KEYWORDS: Phytochemical; antioxidant; anticancer; colon cancer; *Ceratophyllum demersum*

1. INTRODUCTION:

Cancer is a disease described by uncontrolled engendering of cells that have changed from the typical cells of the body. The malignant growth cells can attack the neighbouring and distant tissues via the circulation. In advanced stages, a malignant growth patient may die because of either ill-advised finding or treatment disappointment. Malignancy is one of the push zones for which powerful medications at reasonable costs are not accessible until now presumably because of an absence of understanding the disease pathophysiology. For such a ghastly infection hostile to malignancy drugs have been created from an assortment of sources extending from normal items (plants and organisms) to synthetic particles.

The broadly utilized medications that are malignant growth chemotherapeutic specialists experience the ill effects of the downside of high danger, for example, bone marrow concealment, alopecia, queasiness and spewing and are not inside the compass of a typical man [1,2].

Medicines acquired from plants have assumed a central job in the social insurance of ahead of schedule and late societies. Ayurveda, the Indian arrangement of medication for the most part utilizes plant based medications or formulations to treat different sicknesses including malignancy. About 60% of medications allowed for cancer treatment are of natural source. Vincristine, Etoposide, Irinotecan, Taxanes and Camptothecines are instances of plant-derived anti-cancer compounds. [3,4]

A few malignancies inquire about investigations accompanied using traditional medicinal plants in

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ACADEMIC JOURNALS
African Journal of Pharmacy and Pharmacology

Full Length Research Paper

Anticancer activity of terpenoid saponin extract of *Psidium guajava* on MCF-7 cancer cell line using DAPI and MTT assays

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***Psidium guajava* (Guava) could be an ancient remedy used for a variety of health conditions. Research suggests that guava fruits and leaves might have a variety of advantages. Guava is the tropical tree with yellowish-green skin fruits, and widely grown in Central America and Asia. Individuals use guava leaf tea as a treatment for gastric symptoms in many countries, together with India and China. In different countries, like India and Mexico, individuals have historically used the flesh of the fruit and leaves to heal wounds. Guava leaves extract had shown anticancer, antidiabetic, antispasmodic and anthelmintic effects in various research studies. In our present study, terpenoid saponin, a novel molecule isolated from the fraction of guava leaf extract studied for anticancer activity using 4', 6-diamidino-2-phenylindole (DAPI) and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assays against MCF-7 breast cancer cell line. Terpenoid saponin fraction had shown >60% apoptotic activity using DAPI staining assay against normal cell line activity and shown >99% average %inhibition activity at 400 µg/ml which is a significant result. Thus, we suggest further cell line studies of terpenoid saponin extract of guava leaf for potential anticancer effects and usage.**

Key words: Guava leaves, *Psidium guajava*, terpenoid saponin glycoside, 4', 6-diamidino-2-phenylindole (DAPI), 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), assay.

INTRODUCTION

Psidium guajava is a small tree belonging to the Myrtaceae family popularly known as guava. It is widely available in tropical areas of Southern Mexico, Northern South America and in Asia. Many countries grow guava trees for its fruits allowing mass cultivation in suitable climatic conditions. The fruits are edible and have many medicinal properties and rich in Vitamins like A and C. The leaves are rich in flavonoids and saponins. Many folk

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RESEARCH ARTICLE

Chemopreventive potential of adrenergic blocker in behavioral stress accelerated prostate cancer development in rats

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ABSTRACT:
Psychosocial stress increasingly recognized as an important health issue in development and progression of cancer. Prostate cancer patients have increased levels of stress and anxiety. Several studies suggest that environmental factors are important in prostate cancer development. Patients with prostate cancer reportedly show higher levels of anxiety compared with other cancer patients. Based on psychoneuroimmunology we report that stress promotes prostate cancer in rats through stress response system. The sympathetic nervous system potentially regulate tumour α and β-adrenergic signalling both via circulating adrenaline/nor-adrenaline and via local nor-adrenaline release from SNS nerve fibres. Activation of the sympathetic nervous system promotes cancer progression via β-adrenoreceptor–mediated activation of protein kinase A and exchange protein activated by adenylyl cyclase signalling pathways. Stimulation of α receptor leads to the activation of Ca^{++} permeable no selective cationic channels and transient receptor potential (TRP) channel family, which are responsible for cell proliferation, which leads to prostate cancer progression. Certain adrenergic blockers can exert anticancer activity by blocking α and β adrenergic pathway. Thus current study examined association between prostate cancer progression and behavioural study. Our findings could be used to new clinical and treatment strategies in cancer therapy.

KEYWORDS: stress, cancer, signalling pathway, kinase A, TRP channel family.

INTRODUCTION:

Clinical and epidemiological studies have identified that stress, chronic depression and lack of social support are considered as risk factors for cancer progression.[1-2] Psycho emotional stress activates hypothalamic-pituitary-adrenal axis (HPA) and sympathetic nervous system (SNS) that leads to release of glucocorticoids from adrenal gland, adrenaline and nor-adrenaline from adrenal medulla and sympathetic neurons.[3-4]

According to Reiche E. 2004hypothalamus secretes corticotrophin - releasing factor (CRF) and arginine vasopressin, which activate the HPA axis, leading to release of adrenocorticotrophic hormone, enkephalins, and endorphins.

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The activation of the sympathetic nervous system by CRF is mediated by direct innervation of the locus coeruleus in the brainstem, which leads to widespread release of nor epinephrine throughout the brain and peripheral tissues. Activation of the sympathetic nervous system also stimulates the release of CRF by hypothalamic parventricular nuclei. Thus, activation of one component of the system stimulates the other component.[5]

β adrenergic pathway:[6]

SNS activation regulates cancer-related molecular pathways by direct regulation of β-receptor bearing tumour cells and regulation of other β-receptor bearing cells present in the tumour microenvironment, such as macrophages and vascular cells.β_2 receptor are present on prostate gland cell. Both catecholamines bind to β_2 adrenergic receptor resulting in activation of adenylyl cyclase and subsequent conversion of ATP to cAMP.

European Journal of Medicinal Plants

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Microwave Assisted Extraction of Berberine and Preparation of Berberine Hydrochloride from Berberis Aristata Variety of Nepal, and Quantification using RP-HPLC and HPTLC Methods

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Article

In vitro Antioxidant Potential and Cytotoxicity Study of *Asparagus aethiopicus* L. Extracts on HT-29 Human Colon Cancer Cell Line

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ABSTRACT

Objectives: To decide the phytochemical constituents, antioxidant and anticancer potential of *Asparagus aethiopicus* L. extracts on HT-29 human colon malignant growth cell line. **Methods:** The roots of plant were exposed to Hot Soxhlet continuous extraction with expanding polarity of solvents viz., pet ether, chloroform, ethanol and aqueous maceration. Qualitative phytochemical screening was completed by utilizing distinctive phytochemical tests. The antioxidant potential was tried utilizing 2, 2-diphenyl-1-picrylhydrazyl, ferric ion reducing power assay and phosphomolybdenum assay. *In vitro* anticancer action tried on HT-29 human colon malignant growth cell line and it was assessed by (3-(4, 5-dimethyl thiazole-2yl)- 2, 5-diphenyl tetrazolium bromide) MTT test. **Results and Discussion:** Preliminary qualitative phytochemical screening affirmed the presence of phytoconstituents like alkaloids, flavonoids, glycosides, saponins, sterols, tannins and reducing suger. Antioxidant potential was demonstrated most noteworthy in ethanol extracts dependent on the test performed. The ethanol extracts were seen as an antioxidant and specifically cytotoxic to HT-29 human colon malignant growth cell line. **Conclusion:** The outcomes show that *Asparagus aethiopicus* L. having a potential of antioxidant activity and anticancer action on HT-29 human colon cancer cell line. In any case, further examinations are expected to presume that the particular constituent liable for its antioxidant action and cancer prevention agent.

Key words: Phytochemical, Antioxidant, Anticancer, Colon cancer, *Asparagus aethiopicus.*

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INTRODUCTION

Cancer is a disease described by uncontrolled engendering of cells that have changed from the typical cells of the body. The malignant growth cells can attack the neighbouring and distant tissues via the circulation. In advanced stages, a malignant growth patient may die because of either ill-advised finding or treatment disappointment. Malignancy is one of the push zones for which powerful medications at reasonable costs are not accessible until now presumably because of an absence of understanding the disease pathophysiology. For such a ghastly infection hostile to malignancy drugs have been created from an assortment of sources extending from normal items (plants and organisms) to synthetic particles. The broadly utilized medications that are malignant growth chemotherapeutic specialists experience the ill effects of the downside of high danger, for example, bone marrow concealment, alopecia, queasiness and spewing and are not inside the compass of a typical man.[1] Medicines acquired from plants have assumed a central job in the social insurance of ahead of schedule and late societies. Ayurveda, the Indian arrangement of

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RESEARCH ARTICLE

Polymeric Nanosuspension Loaded Oral Thin Films of Flurbiprofen: Design, Development and *In Vitro* Evaluation

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ABSTRACT:
In the present investigation, effort has been made to stabilize optimized nanosuspension of flurbiprofen through oral thin film formulation. To overcome the issue of stability of nanosuspension and poor bioavailability of flurbiprofen, nanosuspension loaded oral thin films were developed by solvent casting method. Oral thin films can be prepared by simple and scalable method easily. Nanosuspension loaded oral thin films were evaluated for thickness, % moisture absorption and loss, surface pH, weight variation, folding endurance, drug content, disintegration time, *in vitro* drug release and stability. The resultant oral thin films depicted that the particles size range was retained even after their stability study for three months. The dissolution rate of all flurbiprofen oral thin films were significantly increased compared with its marketed oral formulation. Thus it can be concluded that, oral thin films have potential for stabilization of nanosuspension with improved drug release.

KEYWORDS: Oral thin film, Flurbiprofen, Solvent casting method, Nanosuspension, Stabilization.

INTRODUCTION:

Oral route is the most suitable, economical, and common route for drug delivery due high patient compliance and flexibility in the development of dosage form[1-2]. Many drugs exhibit poor aqueous solubility, and oral bioavailability[1-2]. Nanosuspension has potential to enhance aqueous solubility, and dissolution rate but with the challenge of stability[3-4]. Oral thin film (OTF) is a novel dosage form similar to postage stamp in size, shape, and thickness[3-5].These undergo quick disintegration when placed in the mouth without water ingestion or mastication; thus OTF are safe from instability due to pH variations, and enzymes in GI tract[3-6]. Oral thin films have potential for stabilization of nanosuspension with improved drug release. High viscosity of the film prevents aggregation of nanoparticles and drying enhances stability[7].

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Such modified formulation, without changing the chemical structure of drug; are significant to produce quick onset of action during emergency circumstances[7-8]. Flurbiprofen (FBF) is a BCS class II drug belongs to non-steroidal anti-inflammatory drugs (NSAID)[9-10]. It shows low aqueous solubility, and high log P value which is suitable in the development of nanosuspension[9-10]. The present study was aimed to develop stable polymeric nanosuspension loaded oral thin films of flurbiprofen.

MATERIALS AND METHODS:

Materials:

Flurbiprofen (FBF), poloxamer 188 (Pluronic F68), and hydroxypropyl methylcellulose E15 (HPMC E15) were gently given by Sun Pharma Pvt. Ltd. Ahmednagar. Glycerol was procured from Sigma Aldrich. All other chemicals with analytical grade, and double distilled water were used during the research work.

Methods:

Preparation and optimization of flurbiprofen nanosuspension:

FBF loaded nanosuspensions were prepared by nanoprecipitation technique. Accurately weighed FBF and HPMC E15 were dissolved in methanol (co-solvent) by sonication. Above organic phase of drug was added in

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Synthesis of Asymmetric Thiazolyl Pyrazolines as a Potential Antioxidant and Anti-Inflammatory Agents

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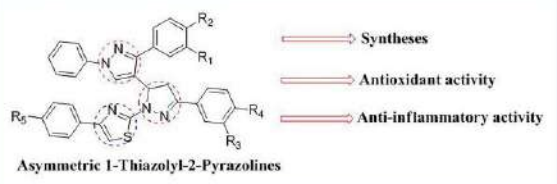
ABSTRACT

A new series of 1-Thiazolyl-2-Pyrazolines **5a-g** was accomplished by reacting pyrazolealdehyde with an appropriate aromatic ketone in the presence of PEG-300 as a solvent to yield chalcone. The chalcones reacted with thiosemicarbazide to yield asymmetric 1-thiocarbamoyl pyrazoles. The above formed 1-thiocarbamoyl pyrazoles reacted with appropriate α- haloketones to yield 1-Thiazolyl-2-Pyrazolines. The structural interpretations of newly formed compounds were done by ^{1}H NMR, ^{13}CNMR, IR and mass spectroscopic methods. The newly prepared asymmetric 1-Thiazolyl-2-pyrazoline derivatives were evaluated to their *in vitro* antioxidant (H_2O_2, DPPH, SOR and NO radical inhibiting activity) as well as anti-inflammatory activity. The 1-Thiazolyl-2-pyrazoline derivatives **5a-g** exhibited moderate to good H_2O_2 scavenging activity as match up to ascorbic acid. All the 1-Thiazolyl-2-pyrazoline derivatives exhibited excellent SOR scavenging activity except **5b**. All the tested compounds have shown good to excellent, NO radical inhibiting activity. DPPH radical scavenging activity results have shown low antioxidant activity. Also, all the 1-Thiazolyl-2-pyrazoline derivatives were tested for their *in vitro* anti-inflammatory activity. The compounds **5a**, **5b**, **5c**, **5f** and **5g** were exhibited good anti-inflammatory activity and **5d** showed moderate activity while **5e** less active as match up to diclofenac sodium as a standard reference.



Asymmetric 1-Thiazolyl-2-Pyrazolines

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KEYWORDS
Anti-inflammatory activity; antioxidant activity; asymmetric 1-thiazolyl-2-pyrazolines; polycyclic aromatic compounds

1. Introduction

Right now our body's cells have face threats every day. The radicals can also cause injury to the smallest structural and functional parts of our body, RNA, DNA and other biomolecules. Out of

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RESEARCH ARTICLE

Design and Evaluation of Eudragit RS-100 Based Itraconazole Nanosuspension for Ophthalmic Application

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ARTICLE HISTORY

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Abstract: ***Background*:** Poor water soluble compounds are difficult to develop as drug products using conventional formulation techniques.

***Objective*:** In the present study, the potential of Eudragit RS-100 nanosuspension as a new vehicle for the improvement of the delivery of drugs to the intraocular level was investigated.

***Methods*:** Solvent evaporation technique has been employed for nanosuspension preparation. Surfactant concentration and drug to polymer ratio has been optimized using 3^2 factorial design to achieve desired particle size, entrapment efficiency and percent permeation responses as dependent variables. All the formulations were characterized for particle size, zeta potential, polydispersity index (PDI), Fourier transform infrared spectroscopy (FTIR), Differential scanning calorimetery (DSC), X-ray diffraction (XRD) analysis, viscosity, antifungal study and Transmission electron microscopy (TEM). Secondly, itraconazole eye drop was prepared by using sulfobuty ether-β-cyclodextrin and comparatively studying its antifungal efficacy.

***Results*:** The nanosuspension had a particle size range of 332.7-779.2nm, zeta potential +0.609-16.3, entrapment efficiency 61.32±1.36%-76.34±2.04%. Ex vitro corneal permeability study showed that optimized Itraconazolenanosuspension produced higher permeation as compared to the market formulation and Itraconazole eye drop. Moreover, optimized nanosuspension was found as more active against *Candida albicans* & *Aspergillusflavus* compared to the market formulation and Itraconazole eye drop.

***Conclusion*:** The nanosuspension approach could be an ideal, promising approach to increase the solubility and dissolution of Itraconazole.

Keywords: Itraconazole, eudragit RS-100, nanosuspension, *Ex-vivo* transconeal permeation.

1. INTRODUCTION

Pertinent information concerning factors affecting drug permeation or retention and eyes anatomy and physiology can be found in several reviews. To penetrate the required amount of drugs into a posterior portion of the eye is the biggest challenge to pharmaceutical scientist due to the complex physiological barrier of the eye without causing permanent tissue damage. A major problem in ocular therapy includes poor drug solubility in lachrymal fluids and repeated instillation of conventional eye drops due to drainage through the nasolacrimal duct [1].

Topical dosage form includes conventional and novel dosages to get maximum ocular bioavailability. Conventional dose forms show loss of drugs *via* nasolacrimal drainage that leads to poor ocular bioavailability such as a solution, suspension and ointment [2]. Novel drug delivery systems for ophthalmic applications such as ocular inserts [3], nanoparticles [4], nanoemulsion [5], nanocapsules [6] and liposomes [7] have been developed to prolong the residence time and improve the bioavailability.

Another issue for lower ocular bioavailability of the drug is its less aqueous solubility. So there is a need for greater awareness about the improvement of solubility by using different techniques like solid dispersion, complexation, liquisolid, hydrotropy, sonocrystallization, self emulsifying method, spherical agglomeration. Among the above discussed various enhancement techniques; a nanosuspension is one of the versatile techniques used to overcome the solubility problem. Recently, nanosuspension, the submicron colloidal dispersion of discrete particles, has been stabilized us-

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RESEARCH ARTICLE

Eudragit RL100 Based Moxifloxacin Hydrochloride and Ketorolac Tromethamine Combination Nanoparticulate System for Ocular Drug Delivery

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ARTICLEHISTORY

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Abstract: ***Background*:** Bacterial conjunctivitis is a serious ocular infection if left untreated. It is caused by several species of bacteria like pseudomonas, staphylococcus and mycobacterium.

***Objective*:** The present investigation explores the development and characterization of moxifloxacin hydrochloride and ketorolac tromethamine combination loaded Eudragit RL 100 nanosuspension for ocular drug delivery in order to overcome the problems associated with conventional dosage forms.

***Methods*:** The nanosuspension prepared by nanoprecipitation technique showed successful entrapment of both water-soluble drugs in the polymer matrix indicated by their % entrapment efficiencies.

***Results*:** Formulations showed a mean particle size <200nm with narrow size distribution and positive surface charge due to the presence of quaternary ammonium groups of Eudragit RL100. FTIR study revealed compatibility among the components, while a reduction in the crystallinity of formulation was observed in the PXRD study. The release of both the drugs was found to be sustained in nanosuspension as compared to commercial eyedrops. *Ex vivo* studies showed increased transcorneal permeation of drugs from nanosuspension, where approximately 2.5-fold and 2-fold increase in the permeation was observed for moxifloxacin hydrochloride and ketorolac tromethamine, respectively. The formulation was stable at 4°C and room temperature.

***Conclusion*:** Due to their sustained release, positive surface charge and higher transcorneal permeation, this will be a promising ocular drug delivery.

Keywords: Drug combination, eudragit RL100, ketorolac tromethamine, moxifloxacin hydrochloride, nanosuspension, ocular drug delivery.

1. INTRODUCTION

Ocular drug delivery is a challenging task due to the unique anatomical, physiological and biochemical features of the eyes. The presence of various barriers prevents the passage of foreign substances as well as drugs into the eyes [1]. Ocular pathological conditions requiring drug delivery to the anterior segment of the eyes are frequently treated with topical instillation of eye drops. Most of the ophthalmic dosage forms are available in the form of solutions for the ease of formulation

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ORIGINAL RESEARCH ARTICLES

ASSESSMENT OF PERMEABILITY BEHAVIOR OF BERBERINE CHLORIDE ACROSS GOAT INTESTINAL MEMBRANE IN PRESENCE OF NATURAL BIOPOTENTIATOR CURCUMIN

Sarika Narade[a]* and Yogesh Pore[b]

(Received 03 October 2019) (Accepted 16 July 2020)

ABSTRACT

The present study investigates the influence of co-administration of different concentrations (2, 6, and 10 mg) of curcumin on goat intestinal permeability of berberine chloride (BBC) using Franz diffusion cell. Data obtained in triplicate from permeability studies were used to calculate percentage cumulative drug release (% CDR), apparent permeability (Papp), flux (J) and enhancement ratio (ER). Co-administration of 6 mg concentration of curcumin with BBC was found to be optimum to enhance the permeability of BBC up to 23.92 ± 0.78 % CDR, over control (8.49 ± 1.45 % CDR). At the optimized concentration of curcumin, permeability characteristics were improved significantly compared to control. The present study reveals the beneficial effect of co-administration of curcumin (6 mg) to promote membrane permeability of BBC which would be expected to improve its bioavailability, thereby therapeutic efficacy. The effect could be attributed to curcumin-mediated inhibition of intestinal efflux pump P-gp, acting as an absorption barrier for BBC.

Keywords: Berberine chloride, permeability studies, curcumin, biopotentiator, co-administration

INTRODUCTION

The natural product berberine chloride (BBC) is a protoberberine alkaloid, having diverse and promising pharmacological actions. It is most widely used since thousands of years in Ayurveda and traditional Chinese medicine for its antiprotozoal, antidiarrheal anti-inflammatory and antimicrobial properties. Recent research has reported that BBC possesses potential therapeutic effects such as antidiabetic, hypolipidemic, anticancer, antiarrhythmic, antifungal, neuroprotective, as well as an anti-atherosclerotic action and improves treatment of polycystic ovary syndrome. In addition, BBC has attracted great interest due to its wide therapeutic applications, cost economy and low toxicity profile[1-5].

However, its oral use has been restricted greatly as it exhibits extremely low and variable plasma concentrations having very poor oral bioavailability (less than 1 %)[2,6]. The low oral bioavailability of BBC might be due to its poor absorption (56 %) and intestinal (43.5 %) as well as hepatic (0.14 %) presystemic metabolism[6]. In addition, drug self-aggregation, decreases solubility in the gastro-intestinal tract, thus, limiting oral absorption of BBC[7]. The low effective permeability coefficient (P_{app} 0.178×10^{-4} cm/s across the rat intestinal mucous membrane) resulting in poor permeability[6], log *P* value -1.5[8] and hepatobiliary re-excretion are major attributions to the poor absorption of BBC[9]. Further, one of the major influencing reasons for poor permeability of BBC is the presence of intestinal multidrug efflux pump P-glycoprotein (P-gp) that acts as an absorption barrier for BBC by active transport of BBC back again into the intestinal lumen and thus, it lowers its permeability as BBC is a substrate of P-gp[10].

Thus, the potential therapeutic uses of BBC have declined significantly due to its low oral permeability and accordingly bioavailability even though it possesses a variety of pharmacological activities. Thus enhancement in the permeability and accordingly bioavailability of BBC seems to be a major challenging task to overcome the problem. This can be solved by effectively limiting the activity of the absorption barrier P-gp.

Till today, to improve permeability and bioavailability of BBC, some studies have explored the use of intestinal

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Research Article

FORMULATION, OPTIMIZATION, AND *IN VITRO* EVALUATION OF POLYMERIC NANOSUSPENSION OF FLURBIPROFEN

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ABSTRACT

Objective: At present, more than 40% of drugs are poorly water-soluble that leads to reduced bioavailability. The objective of the present investigation was to overcome the issue of poor aqueous solubility of drug; therefore, stable flurbiprofen (FBF) nanosuspensions were developed by nanoprecipitation method.

Materials and Methods: Based on particle size, zeta potential, and entrapment efficiency, the polymeric system of hydroxypropyl methylcellulose E15 and poloxamer 188 was used effectively. The prepared formulations were evaluated for Fourier transform infrared spectroscopy, transmission electron microscopy, differential scanning calorimetry, powder X-ray diffraction, saturation solubility, entrapment efficiency, particle size, zeta potential, dissolution profile, and stability.

Results: The resultant FBF nanosuspensions depicted particles in size range of 200–400 nm and were physically stable. After nanonization, the crystallinity of FBF was slightly reduced in the presence of excipients. The aqueous solubility and dissolution rate of all FBF nanosuspensions were significantly increased as compared with FBF powder.

Conclusion: This investigation demonstrated that nanoprecipitation is a promising method to develop stable polymeric nanosuspension of FBF with significant increase in its aqueous solubility.

Keywords: Nanosuspension, Nanoprecipitation, Flurbiprofen, Hydroxypropyl methylcellulose E15, Lyophilization.

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INTRODUCTION

The large number of active pharmaceutical ingredients emerging from the drug discovery process exhibits poor aqueous solubility resulting in a low dissolution rate and oral bioavailability [1,2]. Solubility, dissolution, and permeability of drugs are rate-limiting parameters for its oral absorption [1,2]. Various physicochemical and physiological parameters of drug affect the oral bioavailability of drugs [1,2]. Size reduction of drugs improves oral bioavailability of drug by increasing its effective surface area and thus increasing solubility and dissolution rate of drugs [1,2]. High log p value and molecular weight of the substance are important factors regarding nanosuspension of less aqueous solubility of drugs [2]. Nanosuspension is the novel approach to overcome the problem of low dissolution rate and compromised oral bioavailability and reduce the delivery issues by maintaining the drug in preferred crystalline state [3-8]. Nanosuspension signifies sufficient safety and efficacy [4-6]. According to Nernst-Brunner diffusion layer model, the peripheral layer of the solid particle gets saturated by small portion of an adjacent solvent. Afterward steady-state mass transfer takes place into the bulk solution [8-12]. The formulation can be achieved by top-down (fracturing larger particles to smaller particles) or bottom-up (generation of smaller particles by precipitation at molecular level) approaches [1,9-13]. Nanoprecipitation is one of the promising techniques for the development of nanosuspension of low water-soluble drug molecules [14]. However, particle agglomeration and crystal growth due to Van der Waals forces or Ostwald ripening can be prevented by addition of one or more stabilizer (s) [15]. The selection of polymers and stabilizers is very crucial in the development of nanoformulations. Hydroxypropyl methylcellulose E15 (HPMC E15) and poloxamer 188 (Pluronic F68) are steric stabilizers provide stabilized dispersion by steric hindrance [1,13]. Nanosuspension formulations of several drugs such as Rapamune (sirolimus) and Tricor (fenofibrate) are already successfully marketed [16].

Flurbiprofen (FBF) is a phenylalkanoic acid derivative (Fig. 1), nonsteroidal anti-inflammatory and classified as Biopharmaceutics Classification System Class II drug due to its practical insolubility in water. Its oral bioavailability is affected by low aqueous solubility having pKa value ~ 4.03. The high log p value of FBF is an important feature in the development of its nanosuspension [17,18].

This study was focused to develop stable polymeric nanosuspension for enhancement of dissolution and oral bioavailability of FBF. The solidification of formulations was carried out by freeze-drying.

MATERIALS AND METHODS

Materials

FBF, HPMC E15, and poloxamer 188 (Pluronic F68) were kindly gifted by Sun Pharma Pvt., Ltd., Ahmednagar. Polyvinylpyrrolidone K30 (PVP K30), polyethylene glycol 6000 (PEG 6000), and sodium dodecyl sulfate (SDS) were procured from BASF Ltd. All used supplementary chemicals and reagents were of analytical grade and utilized without additional purification. Double distilled water was used during the experimental work.

Methods

Screening of stabilizer based on settlement volume ratio

To select the optimal stabilizer, the FBF (0.5% w/v) nanosuspensions were prepared using different stabilizers (0.5% w/v) such as PVP K30, PEG 6000, SDS, and poloxamer 188, respectively, by nanoprecipitation technique. The obtained nanoformulations were analyzed by settlement volume ratio (F) for a week, and suitable stabilizer was selected based on the stability of the system [19].

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Design, Development and Characterization of Ketorolac Tromethamine Nanosuspension Loaded *In-Situ* Mucoadhesive Ocular Gel

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ABSTRACT

Currently, a variety of ophthalmic products illustrate low bioavailability after topical administration because of anatomical and physiological barriers of eye. Ketorolac tromethamine (KT) is a BCS class I, potent anti-inflammatory drug. The rationale of present work was to design and develop KT nanosuspension loaded *in situ* gel with sustained effect and greater permeability for ocular drug delivery through increased ocular residence time of drug. KT nanosuspension loaded *in situ* gel was designed by using 3^2factorial design. Polymers and surfactant were optimized through trial batches exhibiting better drug content (%), *In Vitro* trans-corneal permeation (%) and corneal hydration (%).Optimized formulation was evaluated for clarity, pH, gelling capacity, rheological behavior, drug content (%), *Ex-vivo* trans-corneal permeation, corneal hydration, HET CAM assay and physical stability. The resultant formulations revealed optimum viscosity, pH and drug content; as well as higher trans-corneal permeability when compared to the marketed eye drop. Optimized formulation was found as nonirritant to eye with sustained effect and good stability. So, current system can be considered as an efficient ocular drug delivery system for the treatment of postoperative inflammation, which would improve patient compliance and ocular bioavailability.

Keywords: Ketorolac tromethamine, *in situ* gel, corneal hydration, mucoadhesive, trans-corneal permeability

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1. INTRODUCTION

Ketorolac tromethamine (KT) is a BCS class I drug having potent anti-inflammatory activity. Chemically it is a pyrrolizine carboxylic acid; NSAID used for the treatment of post-operative eye inflammation and conjunctivitis[1-2]. Being water soluble agent; to formulate nanosystem is quite difficult by entrapment in polymeric vehicle[3]. Generally the basic problems for topical application in the treatment of ocular infection is drug loss from pre-corneal surface, conjunctival uptake due to poor bioavailability and rapid drainage through naso-lacrimal areas[4-5]. However, short pre-corneal contact time combined with corneal impermeability result in low bioavailability, and frequent dosing is usually needed[6]. Nanosuspension by nanoprecipitation is the novel drug delivery approach for sustaining the drug in its crystalline state[7-9]. Selection of polymers and stabilizers are very essential in the development of nanosuspensions to avoid particle aggregation, and crystal growth[10-11]. Design of experiment has proven effective optimization of formulations[10-11]. In present investigation; formulation was optimized by using 3^2 factorial design. Hence, based on above challenge, KT nanosuspension loaded *in situ* gel increases ocular bioavailability, and residence time on the corneal surface. The rationale of present work was to design and develop KT nanosuspension loaded *in situ* gel with sustained effect and greater permeability for challenging ocular drug delivery.

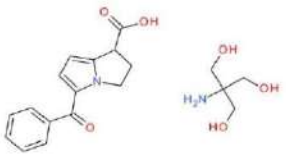

Figure 1: Chemical structure of ketorolac tromethamine

Research Article

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Therapeutic Delivery

Design and evaluation of topical solid dispersion composite of voriconazole for the treatment of ocular keratitis

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Aim: The objective of present investigation was to increases solubility of voriconazole by using solid dispersion techniques and the development of solid dispersion-based voriconazole ophthalmic solutions. **Materials & methods:** The saturation solubility of solid dispersion containing polyvinylpyrrolidone K90 (PVPK-90) was found to increase the solubility of voriconazole compare other carrier like polyethylene glycol and Polyvinylpyrrolidone K 30 (PVPK-30). Solid dispersion of voriconazole was characterized by saturation solubility, Fourier-transform infrared spectroscopy and Differential scanning calorimetry study. **Results & conclusion:** The Fourier-transform infrared spectroscopy and Differential scanning calorimetry studies of voriconazole-based solid dispersion confirmed the complete changes in original polymorphic form of voriconazole. The antifungal assay showed that the maximum zone of inhibition was produced from optimized ophthalmic formulation containing sodium alginate as compared with other formulations and marketed eye drops.

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Keywords: ocular keratitis • PVPK-90 • solid dispersion • transcorneal permeation • voriconazole

Recently, the numbers of drugs are being poorly water soluble and highly lipophilic, resulting in a low bioavailability [1]. Due to this reality, several drug candidates fail to reach the market. About 90% of all new chemical entities have poor bioavailability [1]. Increasing the bioavailability of poorly soluble drugs will be one of the major challenges for the formulation scientists. On the contrary, to achieve the better ocular retention as well as optimum bioavailability, various approaches have been used. Solid dispersion has been widely used to improve drug solubility and bioavailability of poor water-soluble drugs. Some of the existing paradigms are available in the form of solid dispersion like ketoconazole, itraconazole, clotrimazole, terbinafine hydrochloride and miconazole. Solid dispersion technique has been a promising and most successful method in improving the solubility and bioavailability of poorly soluble drugs due to its simplicity and cost-effective. Commonly, the term solid dispersion can be defined as one or more active ingredients in an inert carrier matrix system in solid state prepared by using melting or solvent evaporation method [1]. Some of the earlier literature provides strong evidence about solubility enhancement by using suitable carriers in solid dispersion techniques like levofloxacin [2] and disulfiram [3]. The conventional formulations of the eyes are sometimes unable to treat fungal infections. Fungal keratitis is one of the main causes of ophthalmic mycosis, accounting in some nations for more than 50% of the evidence of ophthalmic mycoses. As per literature, fungal keratitis can lead sever corneal scarring and sometimes loss of vision if it is untreated at early stage [4]. Mostly, this infection is found common in steamy regions and emergent countries [5]. It is need to incorporate drug into the novel drug delivery system. The main reason why topically applied ophthalmic drugs are poor *in vitro* ocular bioavailability is incomplete absorption owing to nasolacrimal drainage [4]. Increased transcorneal preparation of a poorly water-soluble drug may be achieved by formulating solid dispersion-based voriconazole eye drop. Some of the examples are available which has been proof of solubility enhancement and due to this permeation increased by formulating solid dispersion method [6]. Recently, the topical route is the ideal route of administration of antifungal

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Nanostructured lipid carriers (NLC) system: A novel drug targeting carrier

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Bioavailability
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ABSTRACT

Lipid nanocarriers are developed as an alternative to polymeric nanoparticles, liposomes and emulsions. Further, Nanostructured Lipid Nanocarriers are the second generation lipid carriers developed to overcome problems associated with Solid Lipid Nanoparticles and are utilized in various therapeutic approaches. NLCs were primarily considered for the delivery of lipophilic drugs but their suitability for hydrophilic drugs is now well established. Biocompatible nature of lipids is responsible for its development as a promising drug delivery. It was found to be having superior characteristics over other lipid formulations. This article describes the NLC with respect to structures, methods of preparation, characterization, stability and its advantages over first generation lipid nanoparticles. Review mainly focuses on the various therapeutic applications of NLCs and their specificity for different physiological proximities. Due to their biologically non-toxic, non-immunogenic and compatible nature, NLCs are going to be the widely explored lipid nanocarrier systems.

1. Introduction

Exploration of novel lipid nanoparticulate drug delivery system was started from the production of solid lipid nanoparticles (SLNs). Incorporation of drug into various biocompatible lipids formulated at nano range has become a promising approach of drug delivery as lipid nanocarriers. This first generation lipid nanocarrier system was further developed to achieve the drug delivery by numerous routes of administrations in the treatment of physiological complications [1]. Some limitations of SLNs were observed by investigators which resulted into development of new lipid carrier in 1999/2000 by Muller known as nanostructured lipid carriers (NLCs). NLCs were developed by replacing a fraction of solid lipids with liquid lipids to form drug incorporated matrix. Currently, NLCs are considered as potential drug carriers due to their biocompatibility and superior formulation properties over SLNs [2].

Development, characterization and establishment of efficacy of drug loaded NLCs is now a current topic for the drug delivery and targeting. Since most of the drugs are lipophilic in nature, their solubility in biocompatible liquid lipids is a key factor for NLC development. NLCs are explored in the drug targeting in various diseases.

NLCs are developed to improve the oral bioavailability of poorly aqueous soluble drugs [3]. Currently, NLCs incorporated cosmetic products and dermal creams are marketed [4]. Formulation of drugs into NLCs for drug targeting in various diseases is explored widely. Drug targeting to various systems like pulmonary, brain tissues, anterior and posterior ocular tissues [5], targeting cancer tissues in various types of malignancies, improving the bioavailability and specificity and reversal of multidrug resistance is investigated by utilizing NLCs as potential lipid nanocarriers [6]. **Carbone et al** [7] included the information about patents on the lipid based nanocarriers where lipid nanoparticles were developed for the targeting and treatment of various ailments. Oral and topical therapy, brain and cancer targeting, gene delivery are addressed.

1.1. Lipid nanocarriers

SLNs are the first generation lipid nanocarriers. These are developed to formulate drug in solid lipids preferably by cold or hot homogenization technique, depending upon thermal stability of the drug.

Due to some observed limitations of SLNs like drug escape through matrix during storage, lower drug loading efficiency, NLCs were developed. NLC formulation is based on the concept of incorporation of drug in the mixture of varying ratios of solid lipid and liquid lipid. NLCs were designed to obtain the less/no crystalline matrix with solidified core to overcome the limitations occurred due to crystallinity of SLNs core.

Methods of preparation of SLNs and NLCs are not much different from each other. Cold homogenization, hot homogenization, hot emulsification-ultrasonication are the commonly used techniques for

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Optimization of *ex vivo* permeability characteristics of berberine in presence of quercetin using 3^2 full factorial design

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Key words:
Berberine chloride, bioenhancer quercetin, full factorial design, *ex vivo* permeability study, *in vitro* anticancer activity.

ABSTRACT

The aim of the present work was to investigate permeability characteristics of an anticancer berberine chloride, in presence and absence of bioenhancer quercetin on goat intestine using Franz diffusion cell. A 3^2 full factorial design approach was employed to investigate the effect of independent variables such as the concentration of bioenhancer (X_1) and pretreatment time (X_2) on dependent variable % cumulative drug release (% CDR) (Y) using design expert software. The effect of quercetin was examined at three different levels of pretreatment time (30, 45, and 60 minutes) and at three different concentrations (2, 6, and 10 mg) on goat intestine. The apparent permeability (P_{app}), flux (J), and enhancement ratio (ER) were determined. Further, *in vitro* anticancer activity of optimized batch was performed on various cancer cell lines K562, A459, and Hela. During pretreatment studies, it was observed that an increase in the concentration of quercetin yielded a positive effect on % CDR while the increase in pretreatment time by quercetin had a detrimental effect on % CDR. When goat intestine was pre-treated for 30 minutes with 10 mg of quercetin, 90.91% ± 1.66% CDR was obtained while the minimum value of 17.45% ± 2.12% CDR was observed at 2 mg quercetin pre-treated for 60 minutes. *In vitro* anticancer activity of optimized batch demonstrated non-significant effect as compared with parent drug. In conclusion, quercetin could be successfully utilized as bioenhancer to improve *ex vivo* permeability of berberine chloride, which would be expected to improve its bioavailability and reduce the dose resulting in improved patient compliance.

INTRODUCTION

Poor membrane permeation is one of the major governing factors for incomplete oral bioavailability of drugs (Aungst 1993; Savla *et al*., 2017). About 40% of new chemical entities developed in the pharmaceutical industry and more than 80% of drug candidates in research and development pipeline fails because of solubility problems. At present, about 40% of an immediate release oral drugs in the market are practically insoluble (Kawabataa *et al*., 2011; Savjani *et al*., 2012). The solubility and permeability of drug molecule can be correlated with its absorption profile.

Permeability through the gastrointestinal tract is the rate-limiting step for delivering macromolecules and very polar compounds. Poor membrane permeability of drug is attributed to certain physicochemical properties like low octanol/aqueous partitioning, highly polar surface area, high molecular mass, substantial number of hydrogen bonding functional groups, etc., or efflux of drug back into intestinal lumen due to presence of secretory transporters which may include P-glycoprotein (P-gp) and possibly others (Aungst, 2000). In addition to these, as per "Lipinski's rule of 5," if the calculated log P of the drug is more than 5 and the molecular mass is more than 500, then that drug has poor absorption or permeation (Lipinski *et al*., 1997). For oral and intestinal absorption of the drug, the ideal value of log P is 1.35–1.8. Negative value means the drug is more hydrophilic in nature, and thus poorly permeable and bioavailable (Kokate *et al*., 2008). Poorly permeable and bioavailable drugs remain sub-therapeutic as a given dose of drug never reaches to systemic circulation or produces its biological effect after frequent high-dose administration. In such cases, dose escalation would be required which may lead to gastrointestinal toxicity, and thus a reduction in

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RESEARCH ARTICLE

$POCl_3$ Mediated Syntheses, Pharmacological Evaluation and Molecular Docking Studies of Some Novel Benzofused Thiazole Derivatives as a Potential Antioxidant and Anti-inflammatory Agents

Dattatraya G. Raut[1,*], Sandeep B. Patil[2], Prafulla B. Choudhari[3], Vikas D. Kadu[1], Anjana S. Lawand[1], Mahesh G. Hublikar[1] and Raghunath B. Bhosale[1]

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Abstract: ***Background*:** The present research work is focused on the development of alternative antioxidant and anti-inflammatory agents. The review of the literature reveals that many benzofused thiazole analogues have been used as lead molecules for the design and development of therapeutic agent, including anticancer, anti-inflammatory, antioxidant and antiviral. The synthesized benzofused thiazole derivatives are evaluated for *in vitro* antioxidant, anti-inflammatory activities and molecular docking study. Thus, the present research work aims to synthesize benzofused thiazole derivatives and to test their antioxidant and anti-inflammatory activities.

***Objective*:** To design and synthesize an alternative antioxidant and anti-inflammatory agents

***Methods*:** The substituted benzofused thiazoles **3a-g** were prepared by cyclocondensation reaction of appropriate carboxylic acid with 2-aminothiophenol in $POCl_3$ and heated for about 2-3 h to offer benzofused thiazole derivatives **3a-g**. All the newly synthesized compounds were *in vitro* screened for their anti-inflammatory and antioxidant activities by using a known literature method.

***Results*:** At the outset, the study of *in vitro* indicated that the compounds code **3c**, **3d** and **3e** possessed distinct anti-inflammatory activity as compared to a standard reference. All the tested compounds show potential antioxidant activity against one or more reactive (H_2O_2, DPPH, SO and NO) radical scavenging species. Additionally, docking simulation is further performed to the position of compounds **3d** & **3e** into the anti-inflammatory active site to determine the probable binding model.

***Conclusion*:** New anti-inflammatory and antioxidant agents were needed; it has been proved that benzofused thiazole derivatives were **3c**, **3d** and **3e** constituted as an interesting template for the evaluation of new anti-inflammatory agents and an antioxidant's work also may provide an interesting template for further development.

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EVALUATION AND COMPARISON OF ANTIDEPRESSANT ACTIVITY OF MARKETED AYURVEDIC FORMULATIONS

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ABSTRACT:

Depression is referred as an affective disorder which is described by alteration in mood, absence of interest in the surroundings, psychomotor retardation and melancholia. The aim and objectives of present research work is to assess the antidepressant activity and compare the effectiveness of marketed Ayurvedic formulations in mice by using Despair Swim Test and Tail Suspension Test and also estimate the concentration of Nor adrenaline from mouse brain by using Photoflurimeter. The experimental design for present work was the animals were divided into 08 groups and each group contains 06 mice and by using per oral route for 14 days of treatments the Immobility Period was noted on First, Seventh and Fourteenth day.

Forced Swim Test: Group I Control it contains distilled water having dose 10 ml / kg , Group II Standard (Imipramine), dose -15 mg / kg, Group III Formulation A having dose 1.3 ml / kg, Group IV Formulation B dose -1.56 ml / kg. Tail Suspension Test: Group V Control it contains distilled water having dose 10 ml / kg , Group VI Standard (Imipramine), dose -15 mg / kg, Group VII Formulation A having dose 1.3 ml / kg, Group VIII Formulation B dose -1.56 ml / kg. The conclusion of present studies are Formulation A and B possess significant antidepressant activity and Formulation B is highly effective as compared to Formulation A as observed in two models which are employed in this study. However, the precise mechanism of action by which the plants in the formulations shows the antidepressant like effect are not completely studied. So the further additional studies are necessary to isolate the exact active chemical constituents which are responsible for antidepressant action.

KEYWORDS: Depression, Antidepressant drugs, Forced Swim Test, Tail Suspension Test.

INTRODUCTION:

Depression is referred as an affective disorder which is described by alteration in mood, absence of interest in the surroundings, psychomotor retardation and melancholia.[1] Depression belongs to heterogeneous group of mental disorder which is considered by extreme exaggerations and disturbance of mood, which adversely affect cognition and psychomotor functions.[2] The main symptoms of depression are due to functional deficiency in concentration of monoaminergic neurotransmitters like Dopamine, Nor adrenaline, Serotoninin the brain. Those drugs which increases

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ORIGINAL ARTICLE

Production and Quantitative Analysis of Trehalose Lipid Biosurfactants Using High-Performance Liquid Chromatography

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Abstract Trehalose lipids (THL) are glycolipid biosurfactants having a wide range of biomedical and environmental applications. Low yield, high purification cost, and the absence of a valid analytical method hinders their application. Hence, in the present study a simple, rapid, and reliable isocratic high-performance liquid chromatography (LC) method was developed for the identification and quantification of trehalose lipid biosurfactants from *Rhodococcus erythropolis*. THL having a minimum surface tension of 24 mN m^{-1} and a critical micellar concentration of 25 mg L^{-1} were produced using hexadecane as a substrate. A standard was developed from the crude THL mixture using thin-layer chromatography and column chromatography and its structure was confirmed using infrared spectroscopy, mass spectroscopy, and ^{1}H NMR. A high performance liquid chromatography (HPLC) method for quantitation was developed using a C18 column with water/acetonitrile (80:20) as the mobile phase at a 1 mL min^{-1} flow rate and UV detection at 208 nm. This method was validated according to International Conference on Harmonization guidelines for linearity, precision, accuracy, robustness, LOD, and LOQ. This method was found to be linear over the range 10-50 μg m L^{-1} (r^2 =0.99801), precise, accurate, and robust. This method can detect minimum 3.2 μg mL^{-1} and quantify minimum 9.2 μg mL^{-1} of THL. Standards were developed from *R. erythropolis*, broth and purified standard trehalose 6,6′-dimycolate from *Mycobacterium bovis*, having the same retention time of 2.0 min. The yield was calculated from the calibration curve and was found to be 25 g L^{-1}.

Keywords HPLC · Trehalose lipids · Biosurfactants · Surface tension · CMC · Validation

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Introduction

Biosurfactants are biomolecules synthesized by microorganisms, consisting of both hydrophilic and hydrophobic moieties. Biosurfactants reduce surface and interfacial tension between interfaces. Glycolipids, which are monosaccharides or disaccharides acylated with long-chain fatty acids or hydroxyl fatty acids, are the most common among biosurfactants. Rhammnolipids, sophorolipids, mannosylerythritol lipids, and trehalose lipids (THL) are glycolipids that differ in sugar residue in their structure (Fracchia, Cavallo, Martinotti, & Banat, 2012). THL contain trehalose a nonreducing disaccharide, which has two glucose units linked by the α-1,1-glycosidic linkage. Mycolic acids are esterified at the C6 position of each glucose. THL also occurs as mono-, di-, tri-, tetra-, hexa-, and octa-acylated derivatives of trehalose and succinoyl THL (Franzetti, Gandolfi, Bestetti, Smyth, & Banat, 2010). The most reported trehalose lipid is trehalose 6,6′-dimycolate (TDM), which is an α-branched chain mycolic acid esterified at the C6 and C′6 positions of each glucose.

Harshada Patil and Amit Pratap

Studies on Emulsification Properties of Glycolipids Biosurfactants

Microbial biosurfactants consists of hydrophilic and hydrophobic moieties in its structure and are produced by microorganisms. Glycolipid class of biosurfactants has wide range of surface and interfacial properties. The emulsification activity and emulsion stability of the Glycolipids Trehalose lipids (THL), Mannosylerrythritol lipids (MEL), Sophorolipids (SL) and Rhamnolipids (RL) were investigated using liquid paraffin (hydrocarbon source) and sunflower oil (vegetable source) as hydrophobic source by UV spectroscopy. Emulsification activity and stability are in the order THL > MEL > SL > RL. The stability as a function of the temperature in the range of 20 °C–80 °C is in order THL > SL > MEL > RL. The effect of pH was studied using buffers of acidic and basic pH. It was observed that RL and SL had excellent emulsification activity at pH 8 while the activity of trehalose lipids and mannosylerrythritol lipids was not affected by pH. Similar effect of various concentrations of salt (NaCl) was studied; THL and MEL emulsion were very resistant to concentration of salt but the stability of SL and RL emulsion decreased with increased salt concentration. Average droplet diameter of emulsion and the polydispersity index were determined by dynamic light scattering. The emulsions of THL and SL have smallest droplet diameter of 422 nm and 625 nm, while emulsions of MEL and RL have a droplet size of 1923 nm and 2245 nm respectively. Emulsions of all investigatesd glycolipid surfactants had good polydispersity index and negative zeta potential, suggesting their possible applications in pharmaceutical, cosmetics, industrial and environmental techniques.

Key words: Emulsion, glycolipid biosurfactant, emulsifying activity, emulsion stability

Untersuchungen zur Emulgierung von Glykolipid-Biotensiden. Die Moleküle mikrobieller Biotenside bestehen aus hydrophilen und hydrophoben Anteilen und werden von Mikroorganismen hergestellt. Von den Biotensiden haben Glykolipide eine breite Palette von Oberflächen- und Grenzflächeneigenschaften. Die Emulgierfähigkeit und Emulsionsstabilität der Glycolipide Trehaloselipide (THL), Mannosylerrythritollipide (MEL), Sophorolipide (SL) und Rhamnolipide (RL) wurden unter Verwendung von flüssigem Paraffin (Kohlenwasserstoffquelle) und Sonnenblumenöl (pflanzliche Quelle) als hydrophobe Quelle mittels UV-Spektroskopie untersucht. Für die Emulgierungsfähigkeit und Emulsionsstabilität ergibt sich folgende Reihenfolge: THL > MEL > SL> RL. Die Stabilität im Temperaturbereich von 20 °C–80 °C hat folgende Reihenfolge: THL > SL > MEL > RL. Der Einfluss des pH-Werts wurde unter Verwendung von Puffer im sauren und basischen pH-Bereich untersucht. Es wurde beobachtet, dass RL und SL bei pH 8 eine ausgezeichnete Emulgierungsfähigkeit hatten, während die Fähigkeit von THL und MEL nicht durch den pH-Wert beeinflusst wurden. Ein ähnlicher Einfluss von verschiedenen Salzkonzentrationen (NaCl-Konzentrationen) wurde studiert; THL- und SL-Emulsionen blieben bei steigender Salzkonzentration stabil, wohingegen die Stabilität der SL- und RL-Emulsionen mit steigender Salzkonzentration abnahm. Der durchschnittliche Tröpfchendurchmesser der Emulsionen und Polydispersitätsindex wurden durch dynamische Lichtstreuung bestimmt. Die Emulsionen von THL und SL hatten einen kleinsten Tröpfchendurchmesser von 422 nm und 625 nm, während die Emulsionen von MEL und RL einen Tröpfchendurchmesser von 1923 nm bzw. 2245 nm aufweisen. Die Emulsionen aller untersuchten Glykolipidtenside hatten einen guten Polydispersitätsindex und ein negatives Zetapotential, was auf mögliche Anwendungen in der Pharmazie, Kosmetik und in der Industrie- und Umwelttechnik hindeutet.

Stichwörter: Emulsion, Glycolipide, Emulsionsaktivität, Emulsionsstabilität

1 Introduction

Bioemulsifiers and biosurfactants (BS) are amphiphilic biomolecules containing hydrophilic and hydrophobic moiety [1] and are therefore able to display a variety of surface activity like emulsification, dispersion, dissolution, solubilization, wetting and foaming. Bioemulsifier and biosurfactant have advantages in comparison with chemically derived surfactants. These advantages include non toxicity, biocompatibility, biodegradability [2], effectiveness at extreme temperatures, pH, salinity, and at low concentration.

Bioemulsifiers have a higher molecular weight than biosurfactants and are polymers of polysaccharides, lipopolysaccharides, proteins or lipoproteins [3]. Based on the type of the hydrophilic part, biosurfactants are classified into the four categories glycolipids, fatty acids type, lipopeptide and polymer type [4]. Among these biosurfactants the glycolipid type biosurfactants are most intensively studied because their production yield is much higher than that of the other types of biosurfactant. Glycolipid biosurfactants are trehalose lipids, mannosylerythritol lipids, sophorolipids and rhamnolipids [5].

Biosurfactants have numerous applications in medicine as anti-cancer, anti-microbial, anti-viral, anti-adhesive and immunological adjuvants, in cosmetics and food industry, in agriculture, petroleum industry and in microbial enhanced oil recovery (MEOR) [6]. Glycolipid biosurfactants consist of carbohydrate group joined to fatty acids or hydroxyl fatty acid chain.

Trehalose lipids (THL) biosurfactants are commonly produced by *Rhodococcus*, *Cornybacterium*, *Mycobacterium* species. They consist of the disaccharide trehalose which is connected by ester bond to an α branched β-hydroxyl long chained fatty acid. (mycolic acid) [7]. Mannosylerythritol lipids (MEL) are produced by the yeast species *Pseudozyma*, *P. rugulosa*, *P.aphidis* and *P. antarctica*. Mannosylerythritol lipids consist of 4-O-β-D mannopyranosyl-D-erythritol connected to two medium length chains of fatty acyl ester. Sophorolipids (SL) are commonly produced by *Candida bombicola* and *Candida apicola*. Sophorolipids consist of two major types, acidic sophorolipids and lactonic sophorolipids. Acidic sophorolipids have a free carboxlic group in fatty acid

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FORMULATION OF MILD NATURAL BIODEGRADABLE MICRO BEADS FACE SCRUBBER

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Abstract
Daily cleansing does not remove dead epithelial cells and impurities which are trapped in pores of skin. These dead cells and impurities affect the skin life if it trapped in pores of skin resulting the less life of skin, problems of Acne and blackheads. Solution of these problem is use of face scrubber ones or twice in week which is exfoliating, mild and contains natural traditional ingredients.
Generally face scrubber contains crushed seeds for removing dead cells of skin but that crushed seeds are not uniform in size and finely crushed particles causes for skin crashes or damage. To overcome this problem we replace the crushed seeds with granules or beads which removes the dead cells from pores of skin safely and without damaging the skin.
The mild micro beads face scrubber contains Gram flour, aloevera, sugar, starch, milk, Skin care oil etc. in this scrubber-beads are outer cover with Gram flour and inside is oil. When we massage with this beads outer layer are exfoliate dead skin and black heads and inside oils is spread on skin which will help to growth of new fresh cells. The result is ever youthful and fresh look.

Key words: *Mild, Biodegradable micro beads, Natural, exfoliating, youthful and fresh look*

Introduction
Face skin is the major part of the body, which indicates the health of an individual. It consists of materials such as amino acids, lipids and carbohydrates etc so that a balanced nutrition is required for the skin to keep it clear glossy and healthy.
"Mild Natural Biodegradable Micro Beads Face Scrubber" is face scrubber with traditional ingredients in new format. In this scrubber we Replacing crushed seeds with granules or beads in scrubber which contain inner layer of oil which is essential for skin and outer is traditional material gram flour, milk, turmeric and sugar which is bio degradable and natural ingredients which was use traditionally as a cosmetics.
Marketed face scrubber content crushed seeds as a scrubbing material which damage the skin and due to this skin irritation problem are faced by all type of skin. To overcome this problem we replace crushed seeds by micro beads which are uniform in size and round in shape. When beads are rubbed on skin it gives soft feel to skin if in any case damage takes place then it will recover by inner part of beads which is oil and reduce skin damaging
In the present scenario, its need remedy for skin care without side effects. "Mild Natural Biodegradable Micro Beads Face Scrubber" opened the way to formulate cosmetics without harmful effect, which can impart the required properties to remove dead cells from skin pores. This formulation can be