Department: Food Science & Technology

3.4.5

Research papers per teacher in the Journals notified on UGC website

Supporting Documents

Annexure → DFS1-3.4.5

BJPS

Brazilian Journal of Pharmaceutical Sciences

http://dx.doi.org/10.1590/s2175-97902020000118665

Use of microalgal biomass as functional ingredient for preparation of cereal based extrudates: impact of processing on amino acid concentrations and colour degradation kinetics

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Suitability of developing Spirulina incorporated cereal based low cost nutritious extrudates was analysed against extrusion processing parameters. Most significant extrusion processing parameters considered for present study were feed moisture (20-25%), die temperature (100-120 °C) and screw speed (50-100 rpm). Different extrusion conditions were used to obtain most acceptable rice: Spirulina blend extrudates. In present study before extrusion processing different additives (citric acid and sodium bicarbonate) were added in rice: Spirulina blend and checked its effect on colour degradation kinetics at varied packaging and storage conditions. Higher screw speed (100 rpm) indicating less residence time of feed material inside the barrel resulted in higher colour retention of rice: Spirulina (97:03) blend extrudates. Kinetics for rice: Spirulina (97:03) blend extrudates indicates faster rate of colour degradation in terms of lightness (half-life of 4 days) when packed in metalized polyethylene at 50°C with 65% relative humidity. Increased concentration of Spirulina (1-3%) in raw formulations resulted in increase in concentration of all amino acids. Impact of extrusion processing has shown non-significant ($p \leq 0.05$) effect on amino acid concentrations of rice: Spirulina blend extrudates. Also, all the spirulina added samples showed good consumer acceptability with the score of 6.7.

Keywords: Extrusion processing. Spirulina. Storage stability. Colour degradation kinetics.

INTRODUCTION

There is wide spread prevalence of nutritional (protein, vitamins and minerals) deficiency in all risk groups especially among children and women throughout the world. Nutrient deficiencies in developing countries are particularly concerning as these countries are home to more than two-third of the world's total population with a high burden of nutrition-related disease. To address these nutritional deficiencies and prevent their sequelae, extrudates can be used as a medium for incorporating nutrients that have functional importance (Camire, 2011). Snack foods products can be of great economic importance to sustainable agriculture in countries having ever-increasing population pressure and facing resource constraints as well as rapid diminution of natural resources. Potential of extrusion cooking technology for the production of snack foods has long been recognised by food processors globally. It is more effective, cleaner and less expensive with a product of the same quality or even better than manufactured with traditional technologies.

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P-1

Annexure DPST - 3.4.5

Short Communication

Access this article online
Quick Response Code:
Website: www.ijp-online.com
DOI: 10.4103/ijp.IJP_673_17

Cefixime-associated acute generalized exanthematous pustulosis: Rare cases in India

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Submission: 16-11-2017
Accepted: 19-08-2018

Abstract:

BACKGROUND: Cefixime is a widely used third-generation cephalosporin schedule H1 drug, which is prescribed for the treatment of otitis media, respiratory tract infections, and uncomplicated urinary tract infections and is effective against infections caused by *Enterobacteriaceae* and *Haemophilus influenzae* species in India. The National Coordination Centre (NCC)-Pharmacovigilance Programme of India (PvPI), Indian Pharmacopoeia Commission (IPC), has received rare individual case safety reports (ICSRs) for acute generalized exanthematous pustulosis (AGEP) associated with the use of cefixime.

MATERIALS AND METHODS: IPC, NCC-PvPI also acts as a national collaborating center for pharmacovigilance activities under the aegis of Ministry of Health and Family Welfare, Government of India; moreover, it is a member country in global pharmacovigilance system, World Health Organization-Uppsala Monitoring Centre, Sweden. There are more than 250 government/corporate medical colleges and hospitals acting as regional adverse drug reaction monitoring centers, actively functioning under PvPI. Furthermore, various stakeholders including consumers and pharmaceutical industries also play a significant contribution. NCC-PvPI receives spontaneous ICSRs from various stakeholders.

RESULTS: NCC-PvPI, IPC has received a total of four spontaneous ICSRs for cefixime-induced AGEP. After clinical evaluation of reported ICSRs, a strong causal relationship was established between AGEP and cefixime and was supported by published literature and histopathological examination of skin. Based on the statistics with positive information component (IC025 Value: 0.17) and proportionality relative risk (PRR:3.4), PvPI considered cefixime-associated AGEP may be a potential signal.

CONCLUSION: Hence, initially, AEGP is considered by PvPI as drug safety alert in July 2016. Therefore, to enhance the safety of population in rational usage of medication, as a result, there is a need for physicians and health-care professionals to sensitize about serious adverse reaction while prescribing the cefixime as signal in India.

Keywords:

Acute generalized exanthematous pustulosis, cefixime, National Coordination Centre-Pharmacovigilance Programme of India, World Health Organization-Uppsala Monitoring Centre

Introduction

Acute generalized exanthematous pustulosis (AGEP) is a rare cutaneous reaction which advances with multiple pustular lesions on erythematous and edematous surface accompanying with a systemic fever.[1] The European Study of Severe Cutaneous Adverse Reactions study uses scoring scale to distinguish the pustular psoriasis from other pustular eruptions. Approximately 90% AGEP cases were due

How to cite this article: Kumar V, Kalaiselvan V, Kumar AP, Saurabh A, Thota P, Sidhu S, *et al.* Cefixime-associated acute generalized exanthematous pustulosis: Rare cases in India. Indian J Pharmacol 2018;50:204-7.

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21/06/11/21

P-2

Targeted Spontaneous Reporting on Drug Safety Alerts Issued by Pharmacovigilance Programme of India: A New Origin of Pharmacovigilance in India

Sir,

To find out the prevalence among safety alerts issued by National Coordination Centre for Pharmacovigilance Programme of India (NCC-PvPI). The Department of Pharmacology, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, took an opportunity to closely monitor PvPI alerts by implementing targeted spontaneous reporting system on already issued alerts, mentioned in Table 1.

Although PGIMER is functioning as one of the Adverse Drug Reaction (ADR) Monitoring Centre (AMC) under NCC-PvPI, Indian Pharmacopoeia Commission, Ministry of Health and Family Welfare, Government of India, Ghaziabad, since 2010. Furthermore, it is also functioning as a regional training center for pharmacovigilance in the north zone to create awareness among the health-care professionals (HCPs) in reporting ADRs through continuous medical education programs.[1]

Table 1: List of drug safety alerts issued by the National Coordination Centre for Pharmacovigilance Programme of India

Serial number	Suspected drugs	Adverse reactions	Serial number	Suspected drugs	Adverse reactions
1	Phenytoin	Angioedema	31	Olanzapine	DRESS syndrome
2	Phenytoin	Osteoporosis	32	Meropenem	Hypokalemia
3	Nicorandil	Risk of ulcer complication	33	Levamisole	Skin Exfoliation
4	Olanzapine	Hyponatremia	34	Montelukast	Tinnitus
5	Crizotinib	Risk of cardiac failure	35	Cefepime	Dermatitis lichenoid
6	Roflumilast	Gynecomastia	36	Losartan	Burning micturition
7	Clozapine	Neutropenia	37	Deferasirox	Osteoporosis
8	Disulfiram	Erythroderma	38	Ambroxol	Lacrimation
9	Peginterferon alfa-2a	Vasculitis	39	Lurasidone	Thrombocytopenia
10	Piperacillin and Tazobacam	Vision abnormal	40	Etoricoxib	Skin hyperpigmentation
11	Mometasone furoate, topical	Hypertrichosis/hirsutism, skin depigmentation	41	Dexamethasone	Hiccups
12	Ranibizumab	Myocardial infarction	42	Cabergoline	Skin hyperpigmentation
13	Amphotericin B	Bone marrow depression	43	Sodium valproate	Psoriasis
14	Doxorubicin	Photosensitivity reaction	44	Amoxicillin	Eye irritation
15	Crizotinib	Pneumonitis, hepatic encephalopathy	45	Tinidazole	Hyperpigmentation
16	Febuxostat	Allergic vasculitis	46	Amlodipine	Psoriasis
17	Oxcarbamazepine	Hyponatremia	47	Hydroxyzine	Bullous pemphigoid
18	Artemether and lumefantrine	Stevens-Johnson syndrome/toxic epidermal necrolysis	48	Amitriptyline	Gingival discoloration
19	Cefixime	AGEP	49	Paracetamol	Baboon syndrome
20	Hepatitis B immune globulin (human)	Encephalopathy	50	Lamivudine	Hearing loss
21	Cefotaxime	Anaphylactic shock	51	Mebeverine	Retrosternal pain
22	Lacosamide	Red man syndrome	52	Clindamycin	Acute generalized exanthematous pustulosis
23	Dimethyl fumarate	Osteonecrosis	53	Triamcinolone	Skin peeling
24	Sodium citrate/diphenhydramine hydrochloride/ammonium chloride	Myocardial infraction	54	Polymyxin B	Mottled skin
25	Cabergoline	Stevens–Johnson syndrome	55	Diclofenac	Nicolau syndrome
26	Amlodipine	Alopecia	56	Amisulpride	Tinnitus
27	Nitrofurantoin	DRESS syndrome	57	Carbamazepine	Bruxism
28	Cefoperazone sulbactam	AGEP	58	Clomipramine	Melasma
29	Cefixime	Anal ulcer	59	Glimepiride	Lichenoid drug eruption
30	Atenolol	Dermatitis lichenoid	60	Metoprolol	Lichenoid drug eruption

AGEP=Acute Generalized Exanthematous Pustulosis, DRESS=Drug reaction with eosinophilia and systemic symptoms

Annexure DF-59 - 3.4-5
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However, our primary goal is to increase the safety alerts by utilizing already established AMC setup. There are some methods which are employed in the collection of ADRs, a few of which include enclosure of suspected ADR reporting form with inpatients case sheets, using social networking sites, websites, and handouts being placed. Apart from the active surveillance, passive surveillance also plays a pivotal role in present topic of interest. The objective of this study was to analyse the reporting rate of safety alerts by adopting targeted spontaneous reporting methodology, which is a complementary method to routine safety monitoring system. To implement a targeted spontaneous reporting method, initial data are required to support the study; however, in the present scenario, we considered PvPI alerts[2,3] as basic data. We conducted this study to increase the reporting rate on safety alerts to establish the safety signals,[4] and to further communicate to the national database for regulatory inventions.[5] Hence, the information is communicated to all HCPs working at the PGIMER to pay attention during the medical care and treatment while prescribing respective medications.

Acknowledgment

The research facility provided by NCC for PvPI, Indian Pharmacopeia Commission; Department of Pharmacology, PGIMER, Chandigarh; and IKG-Punjab Technical University, Kapurthala, gratefully acknowledged.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Access this article online	
Quick Response Code:	Website: www.jpharmacol.com
	DOI: 10.4103/jpp.JPP_129_18

How to cite this article: Thota P, Sidhu S, Medhi B, Sarma P, Prakash A, Vivekanandan K, *et al.* Targeted spontaneous reporting on drug safety alerts issued by pharmacovigilance programme of India: A new origin of pharmacovigilance in India. J Pharmacol Pharmacother 2019;10:33-4.

Received: 29-11-2018 **Revised:** 23-01-2019 **Accepted:** 01-04-2019

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Annexure PFST- 2019
3.4-5

Available online on 15.04.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

Improved Biological Activity and Stability of enzyme L-Asparaginase in Solid Lipid Nanoparticles Formulation

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ABSTRACT

To protect the biological activity of an enzyme during the development of formulations is one of the biggest challenges. The tetrameric form of L-Asparaginase is used to treat Acute Lymphocytic Leukaemia. It possesses shorter in vivo half-life. Using a modified (water/oil)/water-emulsion method followed by solvent evaporation L-Asn was successfully encapsulated at the core of Solid Lipid Nanoparticles made of lipid glyceryl monostearate. This study elucidated that the preparation of L-Asn loaded SLN develop a colloidal formulation with enhanced activity. The *in-vitro* release profile of the enzyme revealed first bursts has been increased. The study of the lyophilised formulation also shows that the enzyme holds its biological activity and retains its particle size distribution. Consequently, by using the right combination of homogenisation speed, temperature and additives the storage and biological activity of L-Asn in SLN formulation can be improved.

Keywords: L-Asparaginase, Solid Lipid Nanoparticles, Controlled release, Lymphocytic Leukaemia

Article Info: Received 03 March 2019; Review Completed 07 April 2019; Accepted 09 April 2019; Available online 15 April 2019

Cite this article as:

Sharma G, Rath G, Goyal AK, Improved Biological Activity and Stability of enzyme L-Asparaginase in Solid Lipid Nanoparticles Formulation , Journal of Drug Delivery and Therapeutics. 2019; 9(2-s):325-329
http://dx.doi.org/10.22270/jddt.v9i2-s.2708

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1. INTRODUCTION

Proteins are known for their delicate molecular configuration and its relation to their biological activity hence development of a drug delivery system for proteins is an all-time big challenge to the pharmaceutical Industry. Enzyme L-Asparaginase is used specifically in the treatment acute lymphoblastic leukaemia. L-Asparaginase is well known for its ability to catalyse the biochemical reaction that converts proteinogenic amino acid L-Asparagine and produces L-Aspartic Acid and ammonia. This amino acid L-Asparagine is required in the biosynthesis of glycoproteins and other proteins. The ultimate mechanism of action of the L-ASN is that when L-Asparagine that cannot be auto synthesized by cancer cells unlike normal cells and upon degradation in the blood circulation turns to a state of malnourishment and ultimately famishing malignant cells. Short in vivo circulation is one of the prominent problems of L-asparaginase just like other proteins so to meet the desired therapeutic levels it turns inevitable to have multiple intravenous injections [1]. Oscillating L-Asparaginase concentration in the blood accompanying variety of side effects extending from minor allergic reactions to fatal anaphylaxis [2,3]. Anaphylactic authors have also proposed the administration of the L- asparaginase incorporated in liposomes [4-6] Encapsulation protects the protein from its proteolysis and can extend the drug release. This encapsulation as liposomes of as SLN always comes with a biggest challenge of retaining the stability of the protein entrapped and it may be due unfavourable micro environment which interferes the integrity of the protein and affect its biological activity. Encapsulation still at its best loses the biological activity but at the worst can produce immunogenic or toxic products. As an alternative carrier for the delivery of therapeutic proteins, Solid lipid particulate systems have a lot of potential to explore. In this research work an optimum particulate carrier system of Solid Lipid Nanoparticles with L-ASN was developed through optimisation of various parameters. The aim of this research was to incorporate hydrophilic proteins using optimum particulate system formulation and nanospheres (Gaspar et al., 1998). The formulation development process was examined to characterise the influence of optimisation parameters in context to the type and concentration their excipients used, (lipids and surfactants), mechanical parameters like the type of stirrer and speed used and the impact of temperature on the size and biological activity of the enzyme. SLN formulation of L-Asparaginase protects the

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Available online on 15.06.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

Application of Design Of Expert for the Development and Systematic Optimisation of L-Asparaginase loaded Nanoparticulate Carrier Drug Delivery Systems

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ABSTRACT

L-Asparaginase (L-ASN) is a clinically approved chemotherapeutic agent for the treatment of acute lymphoblastic leukaemia and lymphosarcoma. The aim of this research study was to develop and to optimize solid lipid nanoparticle formulation loaded with enzyme L-Asparaginase using response surface methodology (RSM) [1]. The formulation was prepared by a modified double emulsion method followed by solvent evaporation technique using a combination of high-speed homogeniser (10000 rpm) and an automatic hotplate for a temperature 40°C. Box-Behnken Design (BBD) was involved in the study to establish and to understand the relationship between selected design factors and the experimental data thus obtained. A set of 29 formulations were prepared in triplicate based on the recommendations of BBD.[2] The desired results obtained were found to be in close agreement with the experimental results. The responses were fitted to a quadratic; polynomial model. The statistical validation using Analysis of Variance (ANOVA) was done for the respective fitted models.[3] Response Surface Graphs and 3D contour plots were constructed to understand the effect of independent variables in different combinations on the desired responses. SLN prepared were found to be spherical in shape and the mean particle size <198 nm.[4] The polydispersity index (PDI) and the zeta potential recorded for the prepared formulation corresponding to the particle size was 0.096 ± 0.043 and −10.39 mV respectively. The enzyme drug loading was 10.11% ± 2.02 and the enzyme entrapment efficiency was found to be 76.19% ± 1.23. BBD found to be very effective in considering the effects of independent formulation variables to develop an optimised enzyme loaded SLN formulation with sufficient activity of the L-ASN enzyme.

Keywords: Solid Lipid Nanoparticle, Response Surface Methodology, Box-Behnken Design

Article Info: Received 20 April 2019; Review Completed 30 May 2019; Accepted 02 June 2019; Available online 15 June 2019

Cite this article as:

Sharma G, Goyal AK, Singh AP. Application of Design Of Expert for the Development and Systematic Optimisation of L-Asparaginase loaded Nanoparticulate Carrier Drug Delivery Systems, Journal of Drug Delivery and Therapeutics. 2019; 9(3-s):303-308 http://dx.doi.org/10.22270/jddt.v9i3-s.3017

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1.0 INTRODUCTION

Chemically, L-ASN is a tetrameric protein known to produce selective cytotoxic effect on the cancer cells. The cytotoxicity is produced through a hydrolytic reaction catalysed by the enzyme L-Asparaginase. L-Asparaginase is not found in the human blood but it breaks down the essential amino acid L-Asparagine into L-aspartic acid along with the release of ammonia when administered through intravenous route.[5] Unlike normal cells, leukemic cells do not have asparagine synthetase enzyme for the auto synthesis and subsequent replenishment of L-asparagine in cancer cells which leads to its apoptosis. This difference in cellular pathway was scientifically explored to bring selective cytotoxicity of leukemic cells and a breakthrough in the treatment of acute lymphocytic leukaemia (ALL). The enzyme L-Asparaginase was extracted and found effective against ALL for the first time in the year 1953. A chemist J.G. Kidd successfully extracted it from the serum of guinea pig and explore its hydrolytic characteristics [6]. Since then, it has been used to expand life expectancy of leukemic patients. The development of a new anti-cancer drug molecule is a very lengthy and costly venture so working on the betterment and safety efficacy of an existing drug molecule like L-Asparaginase is comparatively a better alternate move. Greater discoveries in the field of drug delivery are also projected in the immediate future. The clinical practice of drug delivery has reformed vividly with the time. Drug Delivery System is an engineered technology, preferably used to get sustained release (control the rate at which a drug is released) and a better targeted delivery (location in the body where it is released) of the anti-cancer drug

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6/10/19

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International Journal of Computer Engineering and Applications
www.ijcea.com, editor@ijcea.com

CERTIFICATE OF APPRECIATION

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have submitted a paper title – **COMPARISON OF IMAGE SEGMENTATION TECHNIQUES: A REVIEW**

The paper was peer reviewed by three blind reviewers. They recommended it to publish in IJCEA issn 2321-3469, Vol.XII, Issue V, May, 2018.

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06/12/18

Annexure DEST-2.4

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Annexure DPST-3.4.5

Rathee et al. Chemistry Central Journal (2018) 12:94
https://doi.org/10.1186/s13065-018-0463-9

Chemistry Central Journal

RESEARCH ARTICLE Open Access

Augmentation of hepatoprotective potential of *Aegle marmelos* in combination with piperine in carbon tetrachloride model in wistar rats

Deepti Rathee[1], Anjoo Kamboj[2] and Shabir Sidhu[3*]

Abstract

The current study investigated hepatoprotective and antioxidant effects of *Aegle marmelos* leaves extract. The major constituent present in the extract i.e. rutin was quantified by using HPLC. Further, the study explored hepatoprotective effect of *A. marmelos* (70% ethanol extract) in combination with piperine. The normal control and carbon tetrachloride (CCl_4) administered rats were divided into 7 groups. Hepatic damage biomarkers were determined in serum samples and oxidative stress biomarkers (malondialdehyde, reduced glutathione, glutathione reductase, glutathione peroxidase, glutathione-S-transferase, superoxide dismutase and catalase), pro-inflammatory and anti-inflammatory cytokines were determined in liver homogenates. CCl_4 caused marked liver damage as evident by significant increased activities of serum alkaline phosphatase, bilirubin, lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase, Interleukin 10 and Tumor necrosis factor-α levels compared to normal control. The oxidative stress parameters also significantly modulated in CCl_4 group as compared to normal control. Treatment with *A. marmelos* reduced the severity of toxicity in a dose dependent fashion and the results of *A. marmelos* extract 50 mg/kg group were comparable to silymarin group. The low dose of *A. marmelos* extract (25 mg/kg) per se did not significantly reversed the hepatotoxicity but low dose of *A. marmelos* in combination with piperine showed significant reversal of hepatotoxicity. In conclusion, *A. marmelos* exerts potential hepatoprotective activity through its antioxidant and anti-inflammatory properties which was enhanced by co-treatment with piperine.

Keywords: *Aegle marmelos*, Rutin, Silymarin, HPLC, Anti-inflammatory, IL-10 and TNF-α levels, Oxidative stress

Introduction

gle marmelos, commonly known as Bael, a spiny tree of Rutaceae family is an indigenous tree found in India, Myanmar, Pakistan and Bangladesh. The leaves, roots, bark, seeds and fruits are edible and have medicinal values. The root is an important ingredient of the 'Dasmula' (ten roots) recipe [1]. Ayurveda describes the medicinal properties of this plant. Ayurvedic literature claims various pharmacological properties of Bael leaves. Activities include astringent, laxative, and expectorant, useful in treatment of ophthalmia, deafness, inflammations, cataract, diabetes, diarrhoea, dysentery, heart palpitation, and asthmatic complications [2]. Increased use of *A. marmelos* as a medicinal agent in different systems of medicine including folk medicine, various research studies undertaken in recent past to explore the therapeutic potential of different parts of the plant. A number of studies showed antifungal [3], ulcer healing [4], anti-inflammatory [5] and anti-diabetic [6] properties of *A. marmelos*. Literature also reports diuretic [7], antifertility [8], hepatoprotective activities [9] and anticancer properties [10].

Economics of treatment, linked to drug dosage, has led to new drug development strategies. Piperine is an amide alkaloid found in the fruits of black and long pepper

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Annexure DFST. 3.4-5

Revista Brasileira de Farmacognosia 28 (2018) 65–72

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Original Article

Hepatoprotective effect of *Aegle marmelos* augmented with piperine co-administration in paracetamol model

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ARTICLE INFO

Article history:
Received 1 August 2017
Accepted 23 November 2017
Available online 15 December 2017

Keywords:
TNF-α
Oxidative stress
Aspartate aminotransferase
Alanine aminotransferase
Bilirubin

ABSTRACT

The current study explored hepatoprotective effect of *Aegle marmelos* (L.) Corrêa, Rutaceae, leaves extract. Potentiation of *A. marmelos* hepatoprotective effect with piperine co-administration was also explored. Wistar rats were randomly divided into seven groups: (i) normal control, (ii) paracetamol group, (iii) silymarin group, (iv) extract-25 group (25 mg/kg body), (v) extract-50 group: (50 mg/kg), (vi) extract-100 group (100 mg/kg) and (vii) extract-25 + piperine group. Hepatotoxicity was induced by administering paracetamol orally in a dose of 400 mg/kg for seven days. The drugs were administered 30 min prior to paracetamol administration and continued for seven days. Animals were 'sacrificed' at the end of treatment and serum was collected for evaluating alkaline phosphatase, bilirubin, lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase IL-10 and TNF-α levels. Liver homogenates were used for determination of oxidative stress (malondialdehyde, reduced glutathione, superoxide dismutase, catalase, glutathione reductase, GSH-S-transferase, glutathione peroxidase and glucose-6-phosphate dehydrogenase). Serum biochemical markers were significantly higher in paracetamol group as compared to normal control group. Significant increase in oxidative stress parameters and inflammatory mediators was also observed. Treatment with *A. marmelos* curtailed the toxic effects of paracetamol in a dose dependent fashion. 100 mg/kg dose of *A. marmelos* was found to be most hepatoprotective. The results of extract-100 group were comparable to silymarin group. Low dose of *A. marmelos i.e.*, 25 mg/kg was combined with piperine to evaluate potentiation of hepatoprotective effects of *A. marmelos*. Piperine co-administration potentiated the hepatoprotective effects, because the combination group results were comparable to high dose *A. marmelos* group. *A. marmelos* exerts hepatoprotective activity through its antioxidant and anti-inflammatory properties which was enhanced by piperine.

Introduction

Liver plays a major role in various stages of biochemical and physiological activities such as energy and nutrient supply, homeostasis, immunity, detoxification as well as metabolism and storage of nutrients (Singh et al., 2016). Industrial toxins, drugs, free radicals, food additives and alcohol are the risk factors for developing liver diseases (Abirami et al., 2015). Drugs causing hepatotoxicity include PCM, NSAID, statins, isoniazid, and various anti-microbial agents (Verma and Neil, 2009). Treatment of drug induced hepatotoxicity is mainly supportive and discontinuation of offending drug is the first step. Certain hepatotoxic drug specific treatments are also available; for example, liver injury due to valproate is treated with carnitine. Likewise, PCM induced liver injury is treated with *N*-acetylcysteine (Leise et al., 2014). Search for newer efficacious hepatoprotective drug fewer side effects is desirable (Mahmood et al., 2014). Recent research has focused on evaluation of hepatoprotective natural products.

Aegle marmelos (L.) Corrêa, Rutaceae, popularly known as Bael in India, is a tough subtropical tree found all over the sub Himalayan forest. The fruits, roots, leaves, bark and seeds of the tree are reported to have medicinal value (Baliga et al., 2011). *A. marmelos* leaves contain large number of phytochemicals such as eugenol, lupeol, cineol, citronellal, cuminaldehyde, skimmianine, citral, aegeline and marmesinine (Maity et al., 2009). *A. marmelos* leaves have been traditionally used in the treatment of fever, cardiac dysfunction, hepatitis, asthma, diabetes, dyspepsia, seminal weakness, inflammation and febrifuge (Sharma et al., 2011). Earlier reports

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https://doi.org/10.1016/j.bjp.2017.11.003

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Annexure DFST- 3.4-5

Drug safety alerts of pharmacovigilance programme of India: A scope for targeted spontaneous reporting in India

Prasad Thota, Anusha Thota[1], Bikash Medhi[2], Shabir Sidhu, Pramod Kumar[1], V. Kalai Selvan[1], Gyanendra Nath Singh[1]

Department of Life Sciences, IKG Punjab Technical University, Jalandhar, Punjab, [1]Indian Pharmacopoeia Commission, Ghaziabad, Uttar Pradesh, [2]Department of Pharmacology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Abstract

Background: The National Coordination Centre-Pharmacovigilance Programme of India (NCC-PvPI), Indian Pharmacopoeia Commission works under the aegis of Ministry of Health and Family Welfare, Government of India. It promotes patient safety in India and also supports postmarketing surveillance programs. Currently, almost hundred thousand case reports are submitted to NCC-PvPI each year through its 250 ADR Monitoring Centers (AMCs) located across India, and India is the one of the top ten contributor countries under WHO-Uppsala Monitoring Centre since 2012 and start issuing drug safety alerts from March 2016.

Aim: This study aims to highlight the drug safety alerts issued by NCC-PvPI from March 2016 to June 2017 and urgent need for further monitoring by adopting targeted spontaneous reporting (TSR) methodology at AMCs and its impact on the NCC's drug safety database, i.e., VigiFlow in India.

Methodology: A retrospective analysis was done for the reported unlisted ADRs by various AMCs to PvPI through VigiFlow, i.e., individual case safety report (ICSR) management system at NCC, where these unlisted drug-ADR combinations considered and issued as drug safety alerts for further reporting these to NCC, if any detected at healthcare settings during routine clinical practice by healthcare professionals.

Results: From July 2011 to June 2017, NCC-PvPI was collated 250,787 ICSRs and contributed to WHO international drug safety database, i.e., VigiBase, from these ICSRs; NCC-PvPI was issued 56 drug safety alerts from March 2016 to June 2017.

Conclusion: In India, spontaneous reporting of ADRs existed since 1998 under passive surveillance method, but there is an urgent need to initiate TSR, which is a complementary method to spontaneous reporting on these drug safety alerts for further regulatory action by Central Drugs Standard Control Organization.

Keywords: Drug safety alerts, pharmacovigilance, Pharmacovigilance Programme of India, spontaneous reporting, targeted reporting

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INTRODUCTION

India is the member country in the WHO Programme for International Drug Monitoring (WHO-PIDM), i.e., WHO-Uppsala Monitoring Centre, Sweden since 1998.[1] Ministry of Health and Family Welfare, Government of India has started a nationwide Pharmacovigilance Programme of India (PvPI) in the year 2010 in All India

Access this article online	
Quick Response Code:	Website: www.picronline.org
	DOI: 10.4103/picr.PICR_29_17

How to cite this article: Thota P, Thota A, Medhi B, Sidhu S, Kumar P, Selvan VK, *et al.* Drug safety alerts of pharmacovigilance programme of India: A scope for targeted spontaneous reporting in India. Perspect Clin Res 2018;9:51-5.

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Annexure DFST-3.4-5 8-5-2018

J Food Sci Technol
https://doi.org/10.1007/s13197-018-3306-8

ORIGINAL ARTICLE

Effect of extrusion on thermal, textural and rheological properties of legume based snack

Laxmi Ananthanarayan[1] · Yogesh Gat[2] · Anil Panghal[2] · Navnidhi Chhikara[2] · Poorva Sharma[2] · Vikas Kumar[2] · Barinderjit Singh[3]

Revised: 16 June 2018 / Accepted: 20 June 2018

Abstract Attempts have been made to improve dough handling properties and quality of legume based snack by incorporating extruded black gram (EBG) flour as partial substitute for raw black gram (RBG) flour. In present work overall quality improvement was achieved by analyzing (a) thermal properties of RBG and EBG flour (b) rheological properties (shear stress, shear rate, storage modulus, loss modulus, deflection angle and complex viscosity) of legume based snack dough and (c) post frying characteristics (colour and texture) of legume based snack. Three different legume based snack samples with different flour formulations (RBG flour, RBG flour incorporated with 25% EBG flour and RBG flour incorporated with 50% EBG flour) were prepared, characterized and compared with standard market sample. Dough exhibited shear thinning behaviour and G′ and G″ showed rising behaviour with angular frequency whereas, complex viscosity showed decreasing behaviour. Herschel–Bulkley model was best fitted. Significant changes were observed in values of onset, peak and endset gelatinization temperatures on extraction of black gram flour which improved dough handling properties during papad processing and enhanced organoleptic profile of end product.

Keywords Black gram flour · Extrusion · Dough rheology · Characterization of legume based snack

Introduction

Extrusion cooking plays a vital role in many processing industries as a continuous cooking, mixing, and forming process which is versatile, low cost, and very efficient technology (Gat and Ananthanarayan 2016). During extrusion processing raw materials has to undergo through many transformations such as starch gelatinization, protein denaturation, complex formation between amylose and lipids, and degradation reactions of vitamins, pigments, etc. (Ding et al. 2005). Moderate starch content in black gram flour favors an extrusion process to produce directly expanded extruded snacks. During extrusion processing of black gram, starch solubilization and gelatinization can be achieved more conveniently and economically without any discoloration. Some of the researchers have worked on use of extruded flour for the quality improvement of idli (Singh et al. 1995; Kaur et al. 2000). Similarly present study was also undertaken for quality improvement of legume based fried snack i.e. papad. In this paper quality improvement of papad was undertaken with use of extruded black gram flour as a partial substitute for raw (un-extruded) black gram flour.

Papad also known as "Appalam" is a legume based popular fried snack item in India. Preparation of papad mainly involves mixing appropriate mixture of black gram (Phaseolus mungo) flour salt and spice powders. Papad dough prepared by adding measured quantity of water into the appropriate mixture of black gram flour is rolled into a circular shape with uniform thickness and then drying to below moisture level 10%. Papads then normally

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Published online: 13 July 2018

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Annexure DFST-3-45

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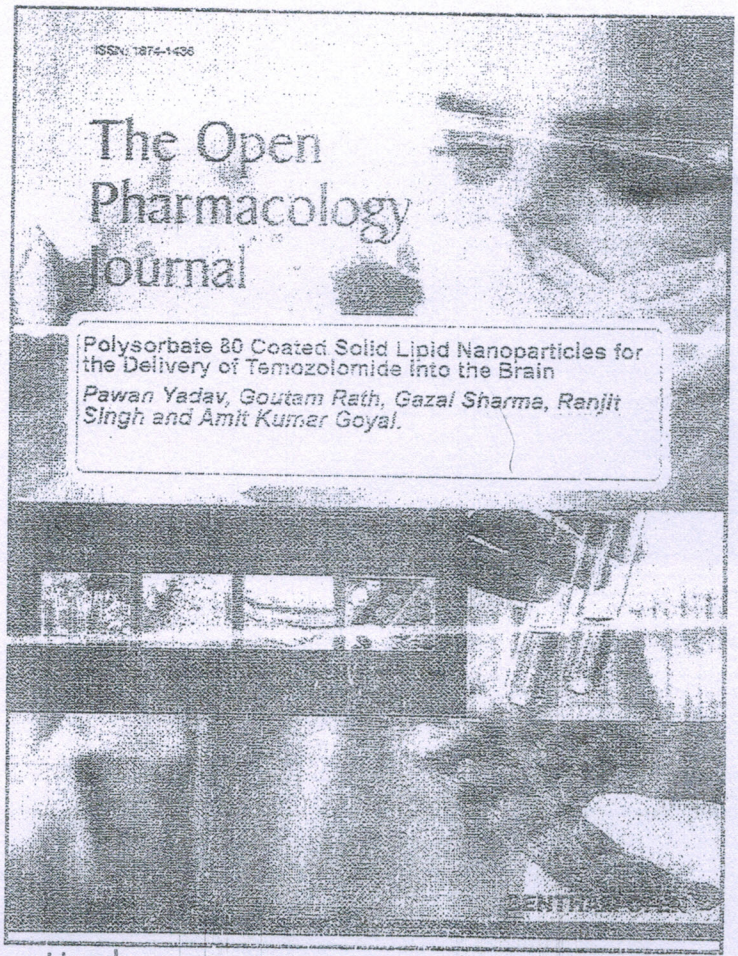

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24/10/21

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G Model
BJP-418; No. of Pages 8

Revista Brasileira de Farmacognosia xxx (2017) xxx–xxx

www.elsevier.com/locate/bjp

Original Article

Hepatoprotective effect of *Aegle marmelos* augmented with piperine co-administration in paracetamol model

Deepti Rathee[a], Anjoo Kamboj[b], Rajneesh Kant Sachdev[c], Shabir Sidhu[c,*]

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ARTICLE INFO

Article history:
Received 1 August 2017
Accepted 23 November 2017
Available online xxx

Keywords:
TNF-α
Oxidative stress
Aspartate aminotransferase
Alanine aminotransferase
Bilirubin

ABSTRACT

The current study explored hepatoprotective effect of *Aegle marmelos* (L.) Corrêa, Rutaceae, leaves extract. Potentiation of *A. marmelos* hepatoprotective effect with piperine co-administration was also explored. Wistar rats were randomly divided into seven groups: (i) normal control, (ii) paracetamol group, (iii) silymarin group, (iv) extract-25 group (25 mg/kg body), (v) extract-50 group: (50 mg/kg), (vi) extract-100 group (100 mg/kg), and (vii) extract-25 + piperine group. Hepatotoxicity was induced by administering paracetamol orally in a dose of 400 mg/kg for seven days. The drugs were administered 30 min prior to paracetamol administration and continued for seven days. Animals were 'sacrificed' at the end of treatment and serum was collected for evaluating alkaline phosphatase, bilirubin, lactate dehydrogenase, alanine aminotransferase, aspartate aminotransferase IL-10 and TNF-α levels. Liver homogenates were used for determination of oxidative stress (malondialdehyde, reduced glutathione, superoxide dismutase, catalase, glutathione reductase, GSH-S-transferase, glutathione peroxidase and glucose-6-phosphate dehydrogenase). Serum biochemical markers were significantly higher in paracetamol group as compared to normal control group. Significant increase in oxidative stress parameters and inflammatory mediators was also observed. Treatment with *A. marmelos* curtailed the toxic effects of paracetamol in a dose dependent fashion. 100 mg/kg dose of *A. marmelos* was found to be most hepatoprotective. The results of extract-100 group were comparable to silymarin group. Low dose of *A. marmelos* i.e., 25 mg/kg was combined with piperine to evaluate potentiation of hepatoprotective effects of *A. marmelos*. Piperine co-administration potentiated the hepatoprotective effects, because the combination group results were comparable to high dose *A. marmelos* group. *A. marmelos* exerts hepatoprotective activity through its antioxidant and anti-inflammatory properties which was enhanced by piperine.

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https://doi.org/10.1016/j.bjp.2017.11.003

Annexure DFST - 3-4-5

Review

Permender Rathee, Anjoo Kamboj and Shabir Sidhu*

Enhanced oral bioavailability of nisoldipine-piperine-loaded poly-lactic-co-glycolic acid nanoparticles

https://doi.org/10.1515/ntrev-2017-0151
Received June 7, 2017; accepted August 4, 2017

Abstract

Background: Piperine helps in the improvement of bioavailability through pharmacokinetic interaction by modulating metabolism when administered with other drugs. Nisoldipine is a substrate for cytochrome P4503A4 enzymes. The study was undertaken to assess the influence of piperine on the pharmacokinetics and pharmacodynamics of nisoldipine nanoparticles in rats.

Methods: Optimization studies of nanoparticles were performed using Taguchi L_9 orthogonal array, and the nanoparticles were formulated by the precipitation method. The influence of piperine and nanoparticles was evaluated by means of *in vivo* kinetic and dynamic studies by oral administration in rats.

Results: The entrapment efficiency, drug loading, ζ potential, and average particle size of optimized nisoldipine-piperine nanoparticles was 89.77±1.06%, 13.6±0.56%, −26.5 mV, and 132±7.21 nm, respectively. The *in vitro* release in 0.1 N HCl and 6.8 pH phosphate buffer was 96.9±0.48% and 98.3±0.26%, respectively. Pharmacokinetic studies showed a 4.9-fold increase in oral bioavailability and a >28.376±1.32% reduction in systemic blood pressure by using nanoparticles as compared to control (nisoldipine suspension) in Wistar rats.

Conclusion: The results revealed that piperine being an inhibitor of cytochrome P4503A4 enzymes enhanced the bioavailability of nisoldipine by 4.9-fold in nanoparticles.

Keywords: bioenhancer; CYP3A4; nisoldipine; optimization; piperine; PLGA.

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1 Introduction

Poly-lactic-co-glycolic acid (PLGA)-based nanocarriers have been extensively explored as drug delivery systems. PLGA is considered to be appropriate for most administration routes [1]. It is approved by the Food and Drug Administration and the European Medicines Agency for application in drug targeting [2, 3]. PLGA, due to its adaptive physical properties, gives flexibility to formulate and accomplish an anticipated dosage form by modifying the molecular weight and lactide/glycolide ratio. Moreover, the metabolism and the kinetics of the active ingredient can be regulated [4–6].

Enhancement of drug bioavailability is always strived for. One of the approaches for enhancing bioavailability is to co-administer drugs with a bioenhancer. Bioenhancers are defined as compounds that themselves are not therapeutic agents but potentiate the therapeutic effect of the co-administered drugs [7]. A number of natural compounds and herbal extracts have the ability to boost the bioavailability by inhibiting metabolism and/or improving absorption [8]. Piperine, obtained from *Piper nigrum*, has been reported to be an excellent bioenhancer [9]. Piperine improves the bioavailability of co-administered drugs by modulating metabolism. It is reported to downregulate or inhibit phase II enzymes like cytochrome P450 isoforms, UDP-glucuronyltransferase, hepatic arylhydrocarbon hydroxylase, and the glucuronidation process in the liver [10–12]. Shoba et al. [13] in 1998 showed a remarkable 2000% increase in curcumin bioavailability by piperine.

Nisoldipine is a second-generation long-acting calcium channel blocker. The vascular selectivity of nisoldipine is 10 times more than that of felodipine, isradipine, and nicardipine, and 100 times more than that of amlodipine and nifedipine [14]. The absolute bioavailability of nisoldipine is about 5% due to high presystemic metabolism in the gut wall and intestine [15]. Cytochrome P4503A4 enzymes are supposed to play a foremost role in the metabolism of nisoldipine [16].

A variety of experimental design methods, like the Taguchi and response surface methodologies, have been

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Annexure DFST-5-45

SHORT COMMUNICATION

Gas chromatography-mass spectrometry analysis of volatile oil obtained from *Aegle marmelos* leaves collected from foothills of Shivalik range

Deepti Rathee[1], AnjooKamboj[2], Shabir Sidhu[3]*

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Abstract

Aim: *Aegle marmelos* (L.) Correa belongs to the Rutaceae family and is abundantly available all over India, and almost every part of this plant is used in traditional medicine. **Materials and Methods:** In the present work, we isolated volatile oil using the standard method of hydrodistillation from the leaves of *A. marmelos*. Further, the analysis of the oil was performed by capillary gas chromatography and gas chromatography-mass spectrometry. **Results and Discussion:** The percentage yield of oil was 0.91 (v/m). Further, the analysis of the oil resulted in the identification of 13compounds comprising more than 85 % of the total oil. The leaf oil was constituted mainly of monoterpene compounds, and the major compounds included a relatively stable terpene-limonene (67.83 %) and caryophyllene (8.76 %).

Key words: *Aegle marmelos*, gas chromatography-mass spectrometry, volatile oil

INTRODUCTION

Traditional or indigenous drugs used by different ethnic groups of the world for treatment of various diseases have special significance of having been tested on wide population over a long time scale. Conventional herbal therapies coupled with dietary measures are prescribed by Ayurveda and other complementary systems of medicines in India as remedies to many ailments in human and animals. A sizeable inhabitant in almost all developed countries uses at least one form of unconventional therapy including herbal medicines.[1,2]

Aegle marmelos Correa (syn. *Feroniapellucida* Roth, *Cratarea marmelos* L., vern. Bael, Vilwam Kuvalam, Bengal Quince, Golden Apple, Stone Apple, and Wood Apple) belongs to the family Rutaceae is a handsome deciduous aromatic tree growing up to 8.5m height which is widely distributed throughout the Indian peninsula along with Sri Lanka, Burma, and Thailand.[3,4] In addition to being regarded as good dietary supplement,[5,6] it has been valued in the treatment of various diseases in complementary systems of medicine.[7] Various parts of the plant have been reported to have a number of bioactive compounds and secondary metabolites belonging to various classes of natural products[8-10] mainly marmenol,[11] marmin,[12] marmelosin, marmelide, psoralen, alloimperatorin, rutaretin, scopoletin.[13-15] aegelin,[16,17] marmelin,[15] fagarine, anhydromarmelin,[18-19] b-carotene, limonene, α-phellandrene, betulinic acid, marmesin,[20] imperatorin[21] marmelosin, luvangentin,[22,23] and auroptene.[24] Many reviews on the plant with special emphasis on pharmacological activities and phytoconstituents have been published in literature.[25-29]

Various studies reported the isolation of volatile compounds from the leaves of *A. marmelos* available in different parts of the world.[30-33] Furthermore, the literature data available from previous publications reported the variation in the amount of volatile oil yield from 0.31% to 1.5% in leaves

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Received: 29-04-2017
Revised: 30-05-2017
Accepted: 18-06-2017

2/06/10/21

P-17

Annexure DFST- 3-4-5

PHARMACEUTICAL BIOLOGY, 2017
VOL. 55, NO. 1, 749–757
http://dx.doi.org/10.1080/13880209.2016.1275023

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RESEARCH ARTICLE

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The novel role of β-aescin in attenuating CCl_4-induced hepatotoxicity in rats

Harsimran Singh[a,b], Shabir Sidhu[c], Kanwaljit Chopra[d] and M. U. Khan[b]

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ABSTRACT

Context: β-Aescin has anti-inflammatory, anti-oxidant and antiedematous properties.

Objective: The present study investigated the hepatoprotective effect and underlying mechanisms of β-aescin in CCl_4-induced liver damage.

Materials and methods: Thirty-five Wistar rats were divided into six groups: normal control, CCl_4 control, silymarin (50 mg/kg, *p.o*) and β-aescin (0.9, 1.8 and 3.6 mg/kg, *i.p.*) treatment for 14 d. CCl_4 (1 mL/kg, *i.p.* for 3 d) was administered to produce hepatic damage. Ponderal changes and liver marker enzymes were estimated. Hepatic oxidative and nitrosative stress was estimated by levels of thiobarbituric acid reactive substances (TBARS), glutathione (GSH) and nitrite/nitrate. Serum TGF-β1 and TNF-α were estimated by ELISA technique. Hepatic collagen and histopathological studies were carried out.

Results: β-Aescin (3.6 mg/kg) markedly decreased CCl_4-induced increased levels of ALT, AST, ALP (71.77 versus 206.7, 71.39 versus 171.82, 121.20 versus 259 IU/L, respectively), total bilirubin (0.41 versus 1.35 mg/dL), TBARS (2.0 versus 8.83 nmol MDA/mg protein), nitrite/nitrate (352.50 versus 745.15 µg/mL) and increased CCl_4-induced decreased GSH levels (0.095 versus 0.048 µmol/mg protein). β-Aescin (3.6 mg/kg) induced focal regenerative changes in liver and markedly decreased TBARS (2.0 versus 8.83 nmol MDA/mg protein), nitrite/nitrate (352.50 versus 745.15 µg/mL), TGF-β1 (92.28 versus 152.1 pg/mL), collagen content (110.75 versus 301.74 µmol/100 mg tissue) and TNF-α (92.82 versus 170.56 pg/mL) when compared with CCl_4 control.

Discussion and conclusion: The findings suggest that β-aescin has a protective effect on CCl_4-induced liver injury, exhibited via its anti-inflammatory, antioxidative, antinitrosative and antifibrotic properties inducing repair regeneration of liver. Hence, it can be used as a promising hepatoprotective agent.

ARTICLE HISTORY
Received 11 October 2015
Revised 22 October 2016
Accepted 17 December 2016

KEYWORDS
Carbon tetrachloride; Silymarin; antifibrotic; oxidative stress; nitrosative stress; *Aesculus hippocastanum*

Introduction

The liver is the largest glandular and vital organ responsible for metabolism of drugs. It plays an instrumental role in detoxifying and excreting numerous xenobiotics and therapeutic agents (Ingale et al. 2014). Injury or destruction to its functions has severe implication to the health of affected person. Administration of carbon tetrachloride (CCl_4) induces hepatotoxicity by generating trichloromethyl (CCl_3^-), a free radical from dehalogenation of CCl_4 by cytochrome (CYP-2E1). This free radical reacts with oxygen to form trichloromethylperoxy (CCl_3OO^-) and stimulates oxidative stress resulting in calcium homeostasis and leading to apoptosis and necrosis (Boll et al. 2001). Further, CCl_4-induced hepatotoxicity involves the overproduction of inducible nitric oxide synthase (iNOS) generated nitric oxide in liver and enhances nitrosative stress and leads to tissue damage (Upur et al. 2009). Moreover, activation of Kupffer cells initiates a cascade of inflammatory mediators by up regulating the expression of nuclear factor kappa B (NF-κB) and subsequently augmenting levels of tumour necrosis factor-α (TNF-α), interleukin (IL)-1β, IL-6, etc. (Ma et al. 2014). In addition, CCl_4 administration increases the deposition of extracellular matrix proteins via increased expression of transforming growth factor-β1 (TGF-β1) and activation of stellate cells. These processes produce fibroblasts and cause hepatic fibrosis and hepatocellular carcinoma, eventually ensuing into liver failure (Huang et al. 2015).

Current available drug treatment is unable to meet the demand clinically due to lack of complete cure, numerous adverse effects, lower safety, etc. Therefore, trends are trickling towards the use of herbal drugs which has a better safety and efficacy profile. β-Aescin is the chief active constituent isolated from the horse chestnut tree *Aesculus hippocastanum* L. (Hippocastanaceae). Traditionally, leaves, bark and seeds were used in the treatment of arthritis, brain trauma, stroke, venous congestion and thrombophlebitis (Celep et al. 2012). Aescin have been reported to possess anti-inflammatory, antiedamatous, antiexudative and antioxidant properties (Xiao & Wei 2005). A large number of studies have reported that decreased levels of IL-6, IL-8, vascular endothelium growth factor and inhibition of NF-κB, matrix metalloproteinase (MMP) and TNF-α may be the plausible mechanisms responsible for anti-inflammatory effect of aescin (Xin et al. 2011; Wang et al. 2013). It is worthwhile to note that sodium aescinate decreases nitrosative stress by suppressing the expression of iNOS (Ji et al. 2011). In addition, aescin has been reported to protect endotoxin-induced liver injury via its

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Annexure DFST- 3.4-5

J Food Sci Technol
DOI 10.1007/s13197-016-2356-z

ORIGINAL ARTICLE

Ultrasound assisted extraction of polyphenols and their distribution in whole mung bean, hull and cotyledon

Barinderjit Singh[1,2] · Narpinder Singh[1] · Sheetal Thakur[1] · Amritpal Kaur[1]

Revised: 19 September 2016 / Accepted: 29 September 2016

Abstract In this study, extraction of polyphenols using different solvents (acetone, ethanol, methanol and water) with ultrasound and conventional method from whole mung bean (WMB), hull and cotyledon was conducted. Total phenolic content (TPC), total flavonoids content (TFC), total antioxidant activities (TAA), ferric reducing power (FRP) and DPPH radical scavenging activity were determined. Ultrasound treated extracts exhibited higher TPC, TFC, TAA, FRP and DPPH in different mung bean fractions than CSE. Among the solvents, acetone showed better TPC, TFC, TAA, FRP and DPPH. Hull had significantly higher TPC, TFC, TAA, FRP and DPPH than WMB and cotyledon. Sinapic acid (SA) was the major polyphenol in different fractions. Acetone extract of hull showed high polyphenol content. SA, ferulic acid, catechin, p-coumaric acid, resveratrol, quercetin and luteolin were the major contributors to antioxidant activity of acetone extract. Mung bean hull contained the maximum polyphenols and acetone was observed to be the best extraction medium for polyphenols in combination with ultrasound.

Keywords Ultrasound · Mung bean · Antioxidants · Optimization · Polyphenols

Electronic supplementary material The online version of this article (doi:10.1007/s13197-016-2356-z) contains supplementary material, which is available to authorized users.

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Introduction

Mung bean is a fast-growing, warm-season Indian originated legume belonging to the family Fabaceae which is also known as *vigna radiate*, green gram, haricot mungo, oregon pea, mungo and chicksaw pea across the globe. The world's 90 % of mung bean is produced by southern and eastern Asian countries followed by Australia, Canada, Southern Europe and Southern United States (Nair et al. 2013; Kim et al. 2015). Mung bean is not only low price legume, rich source of carbohydrates, protein, essential amino acids, minerals and vitamins but it also contains polyphenols like phenolic acids and flavonoids which are beneficial for curing and preventing major chronical ailments viz. cancer, diabetes, cardiovascular diseases due to their antioxidant properties (Luo et al. 2016; Singh et al. 2016). The major polyphenols, such as, caffeic acid, syringic acid, chlorogenic acid, ferulic acid and p-coumaric acid are present in mung bean. These compounds are generally linked to cellulose, lignin and protein through ester bonds (Yao et al. 2013).

The dried seeds of mung bean are consumed either whole or after splitting popularly known as dal or dhal. The splitting of mung bean produces two major milling fractions i.e. cotyledon (75 %) and hull mix (25 % contains seed coat, germ, aleurone layer and plumule). The hull mix is either used as an animal feed or discarded (Girish et al. 2012). But, hull has a high concentration of polyphenols as compared to cotyledon. So, such bio-waste could be used to extract these polyphenols which can be further used as nutraceuticals to cure various ailments in human, in general or food preservation as a natural antioxidant.

Polyphenols can be degraded during conventional solvent extraction (CSE) method due to high temperature, oxidation conditions and/or longer time, therefore, the

Published online: 13 October 2016

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Annexure DFST - 3.4.5

PHARMACEUTICAL BIOLOGY, 2016
http://dx.doi.org/10.1080/13880209.2016.1195848

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

Calendula officinalis ameliorates L-arginine-induced acute necrotizing pancreatitis in rats

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ABSTRACT

Context: *Calendula officinalis* L. (Asteraceae) has been traditionally used in treating inflammation of internal organs, gastrointestinal tract ulcers and wound healing.

Objective: The present study investigates the effect of ethanol extract (95%) of *Calendula officinalis* flowers in L-arginine induced acute necrotizing pancreatitis in rats.

Materials and methods: Rats were divided into four groups: normal control, L-arginine control, *Calendula officinalis* extract (COE) treated and melatonin treated (positive control), which were further divided into subgroups (24 h, day 3 and 14) according to time points. Two injections of L-arginine 2 g/kg *i.p.* at 1 h intervals were administered in L-arginine control, COE and melatonin-treated groups to produce acute necrotizing pancreatitis. Biochemical parameters [serum amylase, lipase, pancreatic amylase, nucleic acid content, total proteins, transforming growth factor-β1 (TGF-β1), collagen content, lipid peroxidation, reduced glutathione and nitrite/nitrate] and histopathological studies were carried out.

Results: COE treatment (400 mg/kg *p.o.*) was found to be beneficial. This was evidenced by significantly lowered histopathological scores (2 at day 14). Nucleic acid content (DNA 21.1 and RNA 5.44 mg/g pancreas), total proteins (0.66 mg/mL pancreas) and pancreatic amylase (1031.3 100 SU/g pancreas) were significantly improved. Marked reduction in pancreatic oxidative and nitrosative stress; collagen (122 μmoles/100 mg pancreas) and TGF-β1 (118.56 pg/mL) levels were noted. Results obtained were comparable to those of positive control.

Discussion and conclusion: The beneficial effect of COE may be attributed to its antioxidant, antinitrosative and antifibrotic actions. Hence, the study concludes that COE promotes spontaneous repair and regeneration of the pancreas.

ARTICLE HISTORY
Received 11 October 2015
Revised 15 May 2016
Accepted 25 May 2016
Published online 23 June 2016

KEYWORDS
Melatonin; oxidative and nitrosative stress; regeneration; TGF-β1

Introduction

Pancreatitis results from an acute injury leading to autodigestion and destruction as a result of activation and release of digestive enzymes in the pancreas (Buchler et al. 2000). Necrotizing pancreatitis is characterized morphologically by tissue edema, acinar necrosis, hemorrhage, fat necrosis and inflammation. Systemic infection, inflammation and multiorgan failure at later stages are responsible for high rate of morbidity and mortality (Davenport 2002). The incidence of pancreatitis is increasing despite improvement in intensive care. However, the treatment for pancreatitis remains supportive and symptomatic (Sidhu et al. 2010). Undiscovered pathogenesis of disease and lack of targeted treatment are equally responsible. Lack of conventional therapy to treat pancreatitis efficiently opens new vistas for development of ethnobotanical drugs.

Calendula officinalis L. (Asteraceae) is commonly known as pot marigold or common marigold. It is grown as a garden plant throughout India. It is used in traditional medicine, especially for wound healing, inflammation of internal organs, jaundice, blood purification and as antispasmodic. *Calendula officinalis* possesses a broad range of activities such as antioxidant, anti-inflammatory, wound healing, antimicrobial, anticancer, antidiabetic, anti-HIV, hepatoprotective and immunostimulant (Arora et al. 2013).

Administration of L-arginine in rats produce pancreatitis by various mechanisms such as increased production of nitric oxide (NO) thereby inducing oxidative and nitrosative stress, increased levels of inflammatory mediators and inducing metabolic acidosis (Hegyi et al. 2004). Based on antioxidant, anti-inflammatory and wound healing properties of *Calendula officinalis*, the current study was undertaken to investigate its potential beneficial effect in acute necrotizing pancreatitis in rats.

Materials and methods

Animals

Sprague–Dawley rats of either sex weighing 180–240 g were used in the present study. The animals were procured from central animal house, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh. They were adapted in the institutional animal house and given rat chow diet (Aashirwad Industries, Mohali, India) and tap water *ad libitum*. They were exposed to normal day and night cycles. The experimental protocol used in the current study was approved by the Institutional Animal Ethics Committee (IAEC) (approval number: IAEC/505). The animal experiments were performed in accordance with guidelines of the committee for

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06/10/21

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J Nat Med
DOI 10.1007/s11418-016-0991-3

ORIGINAL PAPER

Biologically Active Natural Products from Microorganisms and Plants

Protective effect of *Mimosa pudica* L. in an L-arginine model of acute necrotising pancreatitis in rats

Jagdeep Kaur[1,4] · Shabir Sidhu[2] · Kanwaljit Chopra[3] · M. U. Khan[4]

Received: 28 February 2016 / Accepted: 25 March 2016

Abstract *Mimosa pudica* is used in traditional medicine for treating various disorders such as inflammatory conditions, diarrhoea, insomnia, alopecia, urogenital infections and wounds. The present study investigated the effect of *M. pudica* extract (MPE) on L-arginine-induced acute necrotising pancreatitis in rats. The ethanolic extract of *M. pudica* leaves was studied for the presence of quercetin and gallic acid using high-performance liquid chromatography. Four groups were employed—normal control rats, L-arginine control rats (two intraperitoneal [i.p.] injections of 2 g/kg at an interval of 1 h), MPE-treated rats (400 mg/kg orally) and melatonin-treated rats (positive control 10 mg/kg i.p.), which were further divided into subgroups according to time points (24 h, 3 days and 14 days). Serum amylase, lipase, tumour necrosis factor-α (TNF-α), pancreatic amylase, nucleic acid content, protein, transforming growth factor-β1 (TGF-β1), thiobarbituric reactive substances, glutathione, nitrite/nitrate, collagen content and histopathological examination were carried out. MPE significantly improved acute necrotising pancreatitis by modulating diagnostic markers of pancreatitis such as serum lipase and pancreatic amylase, inflammation (TNF-α), and oxidative and nitrosative stress. Moreover, MPE administration induced regenerative changes in the pancreas evidenced by increased levels of pancreatic proteins, nucleic acid content and histopathology report. In addition, MPE improved TGF-β1 and collagen levels thereby preventing fibrosis. The current investigation indicates the novel role of MPE in reducing the severity of acute necrotising pancreatitis by plausible mechanisms such as anti-inflammatory and anti-fibrotic activity and by promoting repair and regeneration of the pancreas.

Keywords L-arginine · *Mimosa pudica* · Pancreatitis · Regeneration

Introduction

Acute pancreatitis is an inflammatory condition of the pancreas characterised by activation of digestive enzymes such as amylase, lipase, release of pro-inflammatory cytokines and pancreatic necrosis [1]. In the pathogenesis of acute pancreatitis, oxidative stress, inflammation and tissue necrosis interplay [2]; however, as its pathogenesis is complicated and poorly understood, only symptomatic and supportive therapy is available [3]. On the other hand, many synthetic and semi-synthetic drugs currently being used for the treatment of acute pancreatitis have their own limitations like high cost, wide adverse effects and unreliability. Hence, there is an urgent need to explore treatment strategies which can combat the above drawbacks. Herbal drugs are among the best option with regard to safety, cost and therapeutic potential [4]. *Mimosa pudica* Linn (Mimosacea) is commonly called the sensitive plant, touch me not, chui mui or laajwanti. The plant contains alkaloids, tannins,

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Published online: 10 May 2016

Annexure DFST-3.1

International Journal of Biological Macromolecules 86 (2016) 556–561

Contents lists available at ScienceDirect

International Journal of Biological Macromolecules

journal homepage: www.elsevier.com/locate/ijbiomac

Optimization and development of Nisoldipine nano-bioenhancers by novel orthogonal array (L27 array)

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ARTICLE INFO

Article history:
Received 23 December 2015
Received in revised form 18 January 2016
Accepted 26 January 2016
Available online 1 February 2016

Keywords:
Statistical array
PLGA
Nisolodipine
Optimization
Development
Nano-bioenhancers

ABSTRACT

Our key objective was an attempt to apply a novel statistical method intended for designing, optimizing and developing Nisoldipine nano-bioenhancers using Taguchi ($3 \times 3 = L_{27}$) design. This quality improvement orthogonal design array (L_{27}) was used as a mathematical tool to find and study the response prediction of independent as well as significant variables (A = poly-concentration; B = bio-enhancer and C = ratio of organic medium). The array orthogonal ($3 \times 3 = L_{27}$) at each level/spaces has been studied with respect to responses changeable (dependent factors); entrapment enhancement (X; evaluated using particle size; Y). All through experimentally performed runs, the results showed independent variables effect individually or simultaneously on changeable (dependent) variables. It also predicted significant variable *via* its "*better to best*" optimized spaces (independent level) and would be considered as novel statistically advanced oral drug delivery vehicle for anti-hypertensive agents.

1. Introduction

There are numerous approaches used to enhance the intestinal absorption of drugs such as absorption enhancers, prodrugs and permeability improving dosage forms such as liposomes and emulsions. Of the promising approaches, the co-administration of therapeutic agents, with natural compounds which helps in .p...ng absorption and modification of the enzymatic degradati... of therapeutic agents has gained great interest in oral drug delivery. Many natural compounds from medicinal plants have demonstrated ability to augment the bioavailability of co-administered drugs by inhibiting efflux pumps or oxidative metabolism, and perturbing the intestinal brush border membrane. Such agents have been defined as Bio-enhancers; "agents which by themselves are not therapeutic entities, but when combined with an active drug lead to the potentiation of the pharmacological effect of the drug" [1,2].

In the 1920s, Bose, reported an enhanced anti-asthmatic effect of an Ayurvedic formula containing vasaka (*Adhatoda vasica*) when administered with long pepper [3]. The term bioavailability enhancer was first coined by Indian Scientists at the Regional Research Laboratory, Jammu (RRL, now known as Indian Institute of Integrative Medicine) discovered and scientifically validated pipeline as the world's first bioavailability enhancer in 1979 [4]. So, there is an increasing interest and medical need for the improvement of bioavailability of a large number of drugs by using non-pharmacological bio-mechanisms [5,6] of bio-agents. Amount of bio-enhancers focused by researchers and found to be active includes: quercetin, genistein, naringin, cinnamon, piperine, glycyrrhizin, niaziridin, zingiberin, Ellison, luteolin, Nitrile glycosides, Indian aloe etc. [7,8]. They are required at low concentrations and also do not possess any pharmacological activity [9]. So, there is an increasing interest and medical need for the improvement of bioavailability of a large number of drugs by using non-pharmacological bio-mechanisms [10].

Nano-bioenhancers are as the nanoparticle forms containing bioenhancers in nanometers size range which can be used as drug delivery vehicles owing to their role in inhibition of metabolic enzymes and easy permeability through the GIT membranes. To overcome first-pass or pre-systemic metabolism problems associated with oral drug-delivery of calcium channel blocking agents, various schemes have been employed to increase the bio-availability of the drugs to maintain a constant plasma concentration for a better healing outcome [10]. The prime research objective was to enhance poor oral bioavailability (due to low aqueous solubility, poor permeability, and rapid first pass hep-

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tp://dx.doi.org/10.1016/j.ijbiomac.2016.01.097
41-8130/

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Annexure DFST - 3-4-5

NRC Research Press

ARTICLE

Hepatoprotective effect of *trans*-Chalcone on experimentally induced hepatic injury in rats: inhibition of hepatic inflammation and fibrosis

Harsimran Singh, Shabir Sidhu, Kanwaljit Chopra, and M.U. Khan

Abstract: The current study investigated the hepatoprotective effect of *trans*-Chalcone in carbon tetrachloride (CCl_4) and paracetamol (PCM) induced liver damage in rats. Administration of CCl_4 and PCM (1 mL/kg, i.p., 3 days, and 2 g/kg, p.o., single dose, respectively) produced hepatic injury. Ponderal changes (percent change in body mass and relative liver mass) and biochemical parameters (serum ALT, AST, ALP, bilirubin) were estimated. The markers of oxidative and nitrosative stress (TBARS, reduced GSH, nitrite and nitrate), hepatic fibrosis (TGF-β1, collagen content), hepatic inflammation (TNF-α), and histopathological study were evaluated. *trans*-Chalcone (5, 10, and 20 mg/kg, i.p.) was found to be beneficial as demonstrated by significant reversal of liver histology by perceptible reduction of inflammatory cell infiltration with regenerative changes in hepatocytes. Improvement in percent change in body mass and significant reduction in relative liver mass were observed. Marked reduction in serum levels of ALT, AST, ALP, and bilirubin were noted. Decreases in TBARS and nitrites and nitrates and increases in reduced GSH levels were noted. Hepatic fibrosis and inflammation were significantly decreased. The findings indicate a novel hepatoprotective role for *trans*-Chalcone by improving hepatic injury by possible actions such as anti-oxidant, anti-nitrosative, anti-fibrotic, and anti-inflammatory. Hence, it can be used as promising hepatoprotective agent.

Key words: trans-Chalcone, paracetamol, carbon tetrachloride, hepatotoxicity, silymarin, fibrosis, inflammation, oxidative stress.

Résumé : Dans les présents travaux, nous avons étudié les effets hépatoprotecteurs de la *trans*-Chalcone dans un modèle de lésions hépatiques causées par le tétrachlorure de carbone (CCl_4) et le paracetamol (PCM) chez le rat. L'administration de CCl_4 et de PCM (à 1 mL/kg par voie i.p. pendant 3 jours et à 2 g/kg par voie orale en dose unique, respectivement) a causé des lésions hépatiques dans les deux cas. Nous avons estimé la variation de poids (le variation en pourcentage du poids corporel, poids relatif du foie) et les paramètres biochimiques (ALT, AST, phosphatase alcaline, bilirubine dans le sérum). Nous avons aussi évalué les marqueurs du stress oxydatif et nitrosatif (TBARS, GSH, nitrite et nitrate), de la fibrose hépatique (TGF-β1, taux de collagène) et de l'inflammation hépatique (TNF-α). L'étude histopathologique a permis d'observer que la *trans*-Chalcone (à 5, 10 et 20 mg/kg par voie i.p.) apportait des bienfaits dont témoignaient la réduction perceptible de l'infiltration de cellules inflammatoires et la présence de changements régénératifs dans les hépatocytes. Nous avons aussi observé une amélioration dans le variation en pourcentage du poids corporel avec une diminution notable du poids relatif du foie. Par ailleurs, nous avons noté une baisse considérable des taux d'ALT, d'AST, de phosphatase alcaline et de bilirubine dans le sérum, ainsi qu'une diminution des taux de TBARS, de nitrites et de nitrates et une augmentation des taux de GSH. Enfin, l'inflammation et la fibrose hépatiques étaient nettement atténuées. Nos résultats font état de nouveaux effets hépatoprotecteurs de la *trans*-Chalcone qui permet d'atténuer les lésions hépatiques, entre autres par des actions anti-oxydantes, anti-nitrosatives, anti-fibrotiques et anti-inflammatoires. Par conséquent, on peut la considérer comme un agent hépatoprotecteur prometteur. [Traduit par la Rédaction]

Mots-clés : trans-Chalcone, paracétamol, tétrachlorure de carbone, hépatotoxicité, silymarine, fibrose, inflammation, stress oxydatif.

Introduction

Liver is an imperative organ that plays a key role in the metabolism of food and drugs. Common disorders of liver include viral hepatitis, fatty liver, cirrhosis, jaundice, fibrosis, liver cancer, and drug-induced hepatic damage (Ingawale et al. 2014). Paracetamol (PCM) is metabolized by hepatic cytochrome (CYP-2E1) to *N*-hydroxyl-paracetamol. At a high dose (2 g/kg), *N*-hydroxy-paracetamol is converted to a highly reactive metabolite *N*-acetyl-*p*-benzoquinoneimine (NAPQI) (Black 1984). This reactive metabolite further oxidizes tissue macromolecules, leading to hepatocellular injury and cell death (McGill et al. 2012). PCM causes liver mitochondrial dysfunction by covalent binding to mitochondrial proteins, resulting in oxidative stress and peroxynitrate formation. Moreover, high doses of PCM produce nitrosative stress by increasing the production of nitric oxide (NO) by stimulating inducible nitric oxide synthase (iNOS) (Chun et al. 2009). Consequently, mitochondrial swelling and cell death occurs due to the opening of a mitochondrial permeability transition pore (James et al. 2003; McGill et al. 2012).

Received 6 February 2016. Accepted 28 February 2016.

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Published at www.nrcresearchpress.com/cjpp on 9 March 2016.

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Total Page - 08.

3.4.5 Number of research papers per teacher in the Journals notified on UGC website during the last five years (15)

3.4.5.1. Number of research papers in the Journals notified on UGC website during the last five years

Title of paper	Name of the author/s	Department of the teacher	Name of journal	Year of publication	ISSN number	Link to the recognition in UGC enlistment of the Journal
Use of microalgal biomass as novel functional ingredient for preparation of cereal based extrudates: impact of processing on amino acid profiling and colour degradation kinetics	LaxmiAnantha narayan, Vikas Kumar, Anil Panghal, **Barinderjit Singh**, RojiWaghmar e, Yogesh Gat and Narinder Kaur	Department of Food Science & Technology, I.K. Gujral Punjab Technical University, Main Campus, Kapurthala	Brazilian Journal of Pharmaceutical Sciences	2020	2175-9790	https://mjl.clarivate.com:/search-results?issn=1984-8250&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal
Cefixime-associated acute generalized exanthematous pustulosis: Rare cases in India	Vipin Kumar, Vivekanandan Kalaiselvan, A. Pramod Kumar, Archana Saurabh, Prasad Thota, **Shabir Sidhu**, Bikash Medhi	Department of Food Science & Technology, I.K. Gujral Punjab Technical University, Main Campus, Kapurthala	Indian Journal of Pharmacology	2019	0253-7613	https://mjl.clarivate.com:/search-results?issn=0253-7613&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal

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DVV DFST-3.45

Targeted Spontaneous Reporting on Drug Safety Alerts Issued by Pharmacovigilance Programme of India: A New Origin of Pharmacovigilance in India	**Shabir Sidhu,** Prasad Thota, , Bikash Medhi, Phulen Sharma, Ajay Prakash, Kalaiselvan Vivekanandan , Anusha Thota	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Journal of Pharmacology and Pharmacotherapeutics	2019	0976-500X	https://mjl.clarivate.com:/search-results?issn=0976-500X&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal
Effect of different drying techniques on chemical composition, color and antioxidant properties of kinnow (Citrus reticulata) peel	**Barinderjit Singh,** Shafiya Rafiq, Yogesh Gat	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Journal of Food Science and Technology	2019	0022-1155	https://mjl.clarivate.com:/search-results?issn=0022-1155&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal
Improved Biological Activity and Stability of enzyme L-Asparaginase in Solid Lipid Nanoparticles Formula	**Gazal Sharma** , Rath Goutamb, Goyal Amit Kumar	Department of Food Science & Technology, I.K. Gujral Punjab Technical University, Main Campus, Kapurthala	Journal of Drug Delivery and Therapeutics	2019	2250-1177	

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Application of Design OfExpert for the Development and Systematic Optimisation of L-Asparaginase loadedNanoparticulate Carrier Drug Delivery Systems	**Gazal Sharma**, Goyal Amit Kumar, Singh A.P	Department of Food Science & Technology, I.K. Gujral Punjab Technical University, Main Campus, Kapurthala	Journal of Drug Delivery and Therapeutics	2019	2250-1177	
Comparision of image segmentation teqniques: A Riview	Sachdev Ezoo, Chopra Vinay, **Sachdev Rajneesh**	Department of Food Science & Technology, I.K. Gujral Punjab Technical University, Main Campus, Kapurthala	International Journal of Computer Engineering and Applications	2018	2321-3469	
Augmentation of hepatoprotective potential of Aegle marmelos in combination with piperine in carbon tetrachloride model in wistar rats	Deepti Rathee, Anjoo Kamboj, **Shabir Sidhu**	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Chemistry Central Journal	2018	2661-801X	https://mjl.clarivate.com:/search-results?issn=2661-801X&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal

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Hepatoprotective effect of Aegle marmelos augmented with piperine co-administration in paracetamol model	**Shabir Sidhu,** Deepti Rathee, Anjoo Kamboj, A. Rajneesh Kant Sachdev,	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Brazilian Journal of Pharmacognosy	2018	0102-695X	https://mjl.clarivate.com:/search-results?issn=0102-695X&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal
Drug safety alerts of pharmacovigilance programme of India: A scope for targeted spontaneous reporting in India	**Shabir Sidhu** ,Thota P, Thota A, Medhi B, Kumar P, Selvan VK, Singh GN	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Perspectives in Clinical Research	2018	2229-3485	https://www.scopus.com/sourceid/21100824459
Effect of extrusion on thermal; textural and rheological properties of legume based snack	**Barinderjit Singh,** Yogesh Gat, Anil Panghal, Navnidhi Chhikara, Poorva Sharma, Vikas Kumar,	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Food Scientists & Technologists	2018	0022-1155	https://mjl.clarivate.com:/search-results?issn=0022-1155&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal

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Polysorbate 80 Coated Solid Lipid Nanoparticles for the Delivery of Temozolomide into the Brain	**Gazal Sharma,** Pawan Yadav, Goutam Rath, Ranjit Singh and Amit Kumar Goyal	Department of Food Science & Technology, I.K. Gujral Punjab Technical University, Main Campus, Kapurthala	The Open Pharmacology Journal	2018	1874-1436	https://www.scopus.com/sourceid/19700175061
Recent Advancement in Nanocarriers for Oral Vaccination	**Gazal Sharma** , Preeti Kour, Goutam Rath, Amit Kumar Goyal	Department of Food Science & Technology, I.K. Gujral Punjab Technical University, Main Campus, Kapurthala	Artificial Cells, Nanomedicine and Biotechnology (IANB)	2018	2169-1401	https://mjl.clarivate.com:/search-results?issn=2169-1401&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal
Hepatoprotective effect of Aegle marmelos augmented with piperine co-administration in paracetamol model	Shabir Sidhu, Deepti Rathee, Anjoo Kamboj, A. **Rajneesh Kant Sachdev,**	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Brazilian Journal of Pharmacognosy	2018	0102-695X	https://mjl.clarivate.com:/search-results?issn=0102-695X&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal

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Enhanced oral bioavailability of nisoldipine-piperine-loaded poly-lactic-co-glycolic acid nanoparticles	**Shabir Sidhu,** Rathee, P. Kamboj, A.	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Nanotechnology Reviews	2017	2191-9089	https://mjl.clarivate.com:/search-results?issn=2191-9089&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal
Gas chromatography-mass spectrometry analysis of volatile oil obtained from Aegie marmelos leaves collected from foothills of Shivalik range	**Shabir Sidhu,** Deepti Rathee, Anjoo Kamboj, A.	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	International Journal of Green Pharmacy	2017	9738-258	https://www.scopus.com/sourceid/19700174900
The novel role of β-aescin in attenuating CCl4-induced hepatotoxicity in rats	**Shabir Sidhu,** Singh, H. Chopra, K. Khan, M.U.	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Pharmaceutical Biology	2017	1388-0209	https://mjl.clarivate.com:/search-results?issn=1388-0209&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal

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Antianxiety Activity of Fractions and Isolated Compounds of Verbena officinalis Aerial Parts	Pawan Kumar, Richa Madaan, Shabir Sidhu	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	International Journal of Pharmaceutical Sciences and Drug Research	2017	0975-248X	https://ugccare.unipune.ac.in/Apps1/User/WebA/SearchList
Ultrasound assisted extraction of polyphenols and their distribution in whole mung bean, hull and cotyledon	**Barinderjit Singh,** Narpinder Singh, Sheetal Thakur, Amritpal Kaur	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Journal of Food Science and Technology	2017	0022-1155	https://mjl.clarivate.com:/search-results?issn=0022-1155&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal
Calendula officinalis ameliorates l-arginine-induced acute necrotizing pancreatitis in rats	**Shabir Sidhu,** Kaur, J., Chopra, K., Khan, M.U.	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Pharmaceutical Biology	2016	1388-0209	https://mjl.clarivate.com:/search-results?issn=1388-0209&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal

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Protective effect of *Mimosa pudica L.* in an l-arginine model of acute necrotising pancreatitis in rats	**Shabir Sidhu,** Kaur, J., Chopra, K., Khan, M.U.	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Journal of Natural Medicines	2016	1340-3443	https://mjl.clarivate.com:/search-results?issn=1340-3443&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal
Optimization and development of Nisoldipine nano-bioenhancers by novel orthogonal array (L27 array)	**Shabir Sidhu,** Rathee, P., Kamboj, A.,	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	International Journal of Biological Macromolecules	2016	0141-8130	https://mjl.clarivate.com:/search-results?issn=0141-8130&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal
Hepatoprotective effect of trans-Chalcone on experimentally induced hepatic injury in rats: Inhibition of hepatic inflammation and fibrosis	**Shabir Sidhu,** Singh, H., Chopra, K. Khan, M.U.	Department of Food Science & Technology, I.K. Gujral Punjab Technical University,Main Campus, Kapurthala	Canadian Journal of Physiology and Pharmacology	2016	0008-4212	https://mjl.clarivate.com:/search-results?issn=0008-4212&hide_exact_match_fl=true&utm_source=mjl&utm_medium=share-by-link&utm_campaign=search-results-share-this-journal

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