The Book of Proceedings

International Conference on Emerging Trends in Pharmaceutical Sciences 2023 (ICETPS 23)

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Message of The General Chair

It is my honor and pleasure to welcome you all to International Conference on Emerging Trends in Pharmaceutical Sciences (ICETPS 23) on March 11, 2023 at Capital University of Science & Technology. It is my great privilege to serve as a General Chair of ICETP 23. The Conference is organized by Faculty of Pharmacy, Capital University of Science & Technology. The ICETPS 23 has provided a multi-disciplinary venue for renowned National & International Scientists and scholars to share their novel ideas and research work about emerging advances in Pharmaceutical Sciences to address the rich space of pharmaceutical problems. The submitted papers were evaluated on the basis of their significance, novelty, and technical quality through critical review process. I am highly thankful to Patron, Mr. Mian Amer Mahmood and Co-Patron, Dr. Muhammad Mansoor Ahmed to extending continuous help and support. I would also like to thank the Organizing Chair of ICETPS 23, Dr. Nadia Shamshad Malik, for the leadership and commitment at the conference. The ICETPS 23 would not have been possible without the enthusiastic and hard work of a different committees of Faculty of Pharmacy. Last, but certainly not least, my thanks go to all the authors and invited speakers who submitted papers and all the attendees of the Conference. I am sure that you will find different sessions of the conference stimulating and a source of inspiration for fuure research.

Dr. Muzaffar Abbas
General Chair ICETPS-23
Dean, Faculty of Pharmacy
Capital University of Science & Technology

Message of The Organizing Chair

Dear Conference Attendees!

It is my pleasure to welcome you all to this year's conference. As the organizing chair, I am thrilled to see so many researchers, professionals, and enthusiasts gather here to exchange ideas and insights on various topics.

Over the course of the conference, you will have the opportunity to attend various presentations, and discussions that cover a wide range of themes. Our esteemed speakers and presenters come from different parts of the country and they bring with them a wealth of knowledge and expertise.

We have put a lot of effort into organizing this conference, and I am confident that it will be a memorable and productive event for everyone involved. I hope that you will take advantage of the opportunity to engage in lively discussions, learn from each other, and build long lasting connections.

Once again, I welcome you all to this conference and wish you a successful and enjoyable time.

Dr. Nadia Shamshad Malik
Organizing Chair ICETPS-23
Faculty of Pharmacy
Capital University of Science & Technology

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Pharmacological evaluations and drug discovery from naturally isolated compound

S. Khan[1]

[1] Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan.

Article Info

Keywords:
Anti-inflammatory Capillarisin;
Anti-nociceptive;
Neuroprotecitve;
Signaling Pathways.

Abstract

Inflammation is a dynamic process with pro-inflammatory mediators and cytokines. A number of drugs have been developed to treat inflammation including agents that reduce the activity of specific mediators and cytokines. In the current study, we are set up to define the molecular targets of naturally occurring natural compounds actions. We investigated that capillarisin produce a marked inhibition of NF-κB and MAP-kinase regulating mediators in various pharmacological models. Capillarisin, chromone derivative from *A. capillaris* exhibits potent anti-inflammatory activity. The capillarisin dose-dependently inhibited the pro-inflammatory mediators in LPS-stimulated RAW 264.7 macrophage and primary macrophages isolated from BALB/c mouse. Molecular analysis using quantitative real time polymerase chain reaction (qRT-PCR) revealed that several pro-inflammatory cytokines, including tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), were reduced by capillarisin, and this reduction correlated with the down-regulation of the NF-κB signaling pathway. Capillarisin suppressed the LPS-induced phosphorylation and degradation of IκBα. Moreover, the MAP-kinase study demonstrated that capillarisin inhibited the p-p38 and p-JNK expressions. To further study the mechanisms underlying its anti-inflammatory activity, an electrophoretic mobility shift assay (EMSA) using a ^{32}P-labeled NF-κB and AP-1 probes were conducted. LPS-induced NF-κB DNA binding was drastically abolished by capillarisin. Furthermore, we also focused on the anti-nociceptive and 7europrotective activities of capillarisin in in vitro and in vivo models. Based on anti-inflammatory properties of capillarisin, various signaling pathways were brought under investigations which demonstrate potent activities in these pharmacological models. Hence, the present data suggest that capillarisn are major anti-inflammatory agent and may be a potential therapeutic candidates for the treatment of inflammatory disorders.

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Drug Utilization Evaluation of Antibiotics in Pediatric Population at a Tertiary Care Hospital

S. Ajaz[1]
[1] Shifa Tameer-e-Millat University, Islamabad, Pakistan.

Article Info

Keywords:
Antibiotics;
Resistance;
Pediatrics;
Stewardship;
Prescribing Indicators;
Drug Interactions.

Abstract

Irrational use of drugs especially antibiotics is a global health issue and it raises the hazard of antibiotic resistance, which ultimately leads to increased length of hospital stay, death rate, and financial burden. Drug utilization evaluation studies are used to monitor drug utilization patterns, antibiotics consumption, adverse drug events, drug interactions, etc. The main aim of this study was to evaluate the drug utilization of antibiotics in the pediatric population at a tertiary care hospital. A retrospective descriptive cross-sectional study was designed to evaluate drug utilization of antibiotics in the pediatric population at Shifa International Hospital, Islamabad Pakistan. The study population included all the pediatric patients admitted to the hospital from January 2022 to March 2022. A total of 754 patients' prescriptions were reviewed. Data about drugs, antibiotics and injectables prescribed and drug interactions were extracted from the MIS. Demographics like age, gender, length of stay, and diagnosis were recorded as well. Using this data drug interactions were also evaluated. Data were analyzed by entering in Microsoft Excel and after clean coding, the data was transferred to SPSS version 22. For descriptive analysis frequencies and other parameters were computed to determine prescribing indicators and the prevalence of drug interactions. Kruskal-Wallis (one-way ANOVA) test was performed to compare different antibiotics consumption among wards. <0.05 was considered a statistically significant P-value. Results showed that an average of 6.9 drugs were prescribed per encounter, encounters with antibiotics prescribed were 77% and the percentage of encounters with injections was 91% which was very high compared to the WHO standard. DOT of antibiotics was measured which showed that the most frequently used antibiotic was ceftriaxone. Drug interactions were also evaluated which highlighted that out of a total of 754 prescriptions 41% (n=312) had at least one drug interaction in them. Out of a total of 1603 interactions, 2% were category X, 19% were category D, 58% were category C and 20% were category C interactions. The most frequently occurring drug interaction was between acetaminophen and ondansetron which accounted for 11% (n=84) of total interactions. Drug utilization evaluation showed overutilization of antibiotics in the pediatric population. All three prescribing indicators assessed in this study showed inappropriate values in comparison to WHO optimal range.

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Nanoemulsion Based Dissolving Microneedle Arrays for Enhanced Intradermal and Transdermal Drug Delivery

M.I. Nasiri[1,2], L. K. Vora[1], J. A. Ershaid[1], K. Penga1, I. A. Tekko[1], and R. F. Donnelly[1]
[1]Queens University Belfast, School of Pharmacy, Belfast, UK
[2]Faculty of Pharmacy, Hamdard University, Islamabad, Pakistan

Article Info

Keywords:
Nanoemulsion, Dissolving-Microneedles, Synergistic Effect, Amphotericin B, Transdermal Delivery.

Abstract

Transdermal drug delivery is a beneficial means of administration of therapeutic molecules, as it bypasses first-pass metabolism associated with oral administration. Microneedles (MN) are micron-scale projection arrays (50μm– 900μm), which can painlessly penetrate the skin (stratum corneum) to facilitate intradermal delivery of drugs and vaccines. For the first, in the history of microneedles, nanoemulsion (NE) based dissolving MN were prepared using biocompatible and biodegradable polymers with good mechanical properties. Polyvinyl alcohol and polyvinyl pyrrolidine were used in the MN casting. Campul MCM-8 was used as oil phase (antifungal activity) which produced synergistic affect with Amphotericin B (AmB). This research work describes the feasibility of intradermal and transdermal delivery of model drug using dissolving microneedles. The novel dissolving MN was designed to facilitate intradermally as well as transdermal delivery of drug loaded NE. The solubility of AmB in different oils, lipids, fatty acid, surfactants, and water was assessed by dissolving an excess amount of AmB in each component. In-situ AmB NE were prepared directly mixing the Campul-MCM-8/Tween-80/AmB/DMSO components into Polyvinyl alcohol (PVA) (40% w/w) and polyvinyl pyrrolidine (PVP) (60% w/w) for microneedle casting. NE was characterised for droplet size, polydispersibility index (PDI), zeta potential, TEM analysis, and stability studies. The morphology (droplet size and shape) of drug-loaded NE, drug-free NE, and DMN were assessed using transmission electron microscopy (TEM). Results revealed that NE-based DMN patch with pyramidal tips and baseplate containing high drug loading (~ 427 μg/patch). DMN arrays were strong enough to penetrate up to 4th layer of Parafilm M® and excised porcine skin models and showed good strength (reduction in height <1.4%) after application of 32 N force. The developed DMN arrays illustrated 100% dissolution of needles within 25 min after insertion into excised porcine skin and substantial amounts of 111 ±48.4 μg/cm2 (13% of loaded dose) after 24 h were deposited in the skin. Zone of inhibition (ZOI) values for group-A (68.75 ±4.79 mm) was significantly greater than group-D (51.0 ±5.29 mm) and group-C. This significantly high activity of drug loaded DMN may be due to the synergistic activity of oil (campul-MCM C-8) used in the formulation development of nanoemulsion. This is the first

time a NE of a hydrophobic model drug was successfully optimized and incorporated into DMN arrays, to penetrate the skin and dissolve rapidly in the skin to achieve effective drug permeation.

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1,2,4-Triazole and 2-Methylbenzimidazole Derivatives as α-Glucosidase Inhibitors: Synthesis, In-Silico Studies and Biological Evaluation

T. Waseem[1,2], M. Ahmed[2], and T. A. Rajput[2]

[1]Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan

[2] Shifa College of Pharmaceutical Sciences, Faculty of Pharmaceutical & Allied Health Sciences, Shifa Tameer-e-Millat University, Islamabad, Pakistan

Article Info

Keywords:
Diabetes,
In-Silico,
Biological,
1,2,4-Triazole,
2-Methylbenzimidazole,
Bioavailability.

Abstract

Inflammation is a dynamic process with pro-inflammatory mediators and cytokines. A number of drugs have been developed to treat inflammation including agents that reduce the activity of specific mediators and cytokines. In the current study, we are set up to define the molecular targets of naturally occurring natural compounds actions. We investigated that capillarisin produce a marked inhibition of NF-κB and MAP-kinase regulating mediators in various pharmacological models. Capillarisin, chromone derivative from A. capillaris exhibits potent anti-inflammatory activity. The capillarisin dose-dependently inhibited the pro-inflammatory mediators in LPS-stimulated RAW 264.7 macrophage and primary macrophages isolated from BALB/c mouse. Molecular analysis using quantitative real time polymerase chain reaction (qRT-PCR) revealed that several pro-inflammatory cytokines, including tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), were reduced by capillarisin, and this reduction correlated with the down-regulation of the NF-κB signaling pathway. Capillarisin suppressed the LPS-induced phosphorylation and degradation of IκBα. Moreover, the MAP-kinase study demonstrated that capillarisin inhibited the p-p38 and p-JNK expressions. To further study the mechanisms underlying its anti-inflammatory activity, an electrophoretic mobility shift assay (EMSA) using a 32P-labeled NF-κB and AP-1 probes were conducted. LPS-induced NF-κB DNA binding was drastically abolished by capillarisin. Furthermore, we also focused on the anti-nociceptive and 11europrotective activities of capillarisin in in vitro and in vivo models. Based on anti-inflammatory properties of capillarisin, various signaling pathways were brought under investigations which demonstrate potent activities in these pharmacological models. Hence, the present data suggest that capillarisn are major anti-inflammatory agent and may be a potential therapeutic candidates for the treatment of inflammatory disorders.

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Fabrication and Evaluation of Alginate Based Microparticles for Controlled Delivery of Loxoprofen Sodium

K. Ullah[1], S. A. Khan[2], and M. Mehboob[2]

[1]Faculty of Pharmacy, Hamdard University, Islamabad Campus, Pakistan

[2]Department of Pharmacy, Comsats University Islamabad, Abbottabad Campus, Pakistan

Article Info

Keywords:
Sodium Alginate, Glutaraldehyde, Loxoprofen Sodium, Emulsification, Microparticles, Drug Release.

Abstract

To fabricate sodium alginate based microparticles for controlled delivery of loxoprofen and investigate the effect of process variables on particle size, encapsulation efficiency, percent yield and micromeritic properties of the prepared microparticles. Sodium alginate based microparticles were prepared by water-in-oil (W/O) emulsification method using Glutaraldehyde as crosslinker. The microparticles were characterized using Fourier transform infrared spectroscopy (FT IR), Differential scanning calorimetry (DSC) and Scanning electron microscopy (SEM). The microparticles were also investigated for entrapment efficiency, percent yield, mean particle size and loxoprofen release. Increasing polymer ratio resulted in increased encapsulation efficiency (97.9±0.9%), increase yield (91.1±0.31%) and increased particle size (80.91±0.05µm). Increase in crosslinker concentration resulted in decreased encapsulation efficiency (80.8 ±0.2%), increase in yield (94.5 ± 0.51%) and decrease particle size (69±0.05µm). while increasing the crosslinking time resulted in decreased encapsulation efficiency (76.1 ±0.6%), increase yield (90.1± 0.82%) and increased particle size (84.56±0.07µm). FT IR spectra confirmed physical interaction of loxoprofen with sodium alginate while DSC graphs revealed thermal stability of the prepared microparticles. SEM micrographs showed that microparticles have smooth surface with irregular shapes. Drug release mechanism was non-Fickian. Formulation of loxoprofen using sodium alginate produces controlled drug delivery that can effectively deliver the drug.

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Design, Synthesis and Pharmacological Investigation of Novel Benzimidazole Derivatives as Anti-ulcer Agents

H. A. A[1]. Kharl[1] and H. Nadeem[1]

[1]Riphah Institute of Pharmaceutical Sciences, Riphah International University, Islamabad, Pakistan

Article Info

Keywords:
2-Mercaptobenzimidazole,
Ulcer,
H/K ATPase,
Carbonic Anhydrase,
Ethanol Induced Ulcer.

Abstract

Ulcer may develop at any area of elementary canal including esophagus, stomach, duodenum or other. Any imbalance leads to destruction of mucosal lining of gastrointestinal tract resulting in peptic ulcer. The unique structural features of benzimidazole and a wide range of biological activities of its derivatives made it a privileged structure in drug discovery. Objectives of the study were design of novel benzimidazole derivatives, Docking of designed inhibitors with (H+/K+) ATPase, COX-II and CA-II enzyme and determination of in-vitro (H+/K+) ATPase, CA-II and COX-II inhibitory activity in-vivo anti-ulcer and acute toxicity of synthesized derivatives. Briefly 20 different chalcones were prepared by reacting substituted aldehydes with ketones, these chalcones were condensed with benzimidazole-pyrazole hybrids to give final products (M3a–M3t). Docking and In-silico studies were done by utilizing AutoDockVina and online tools (SWISS ADME). Different enzymes including CA-II and H+/K+ ATPase to visualize binding affinity of respective ligand to enzymes. The results showed that all of the compounds were analyzed for Lipinski's rule of five, among these compounds none of the compound deviate from this rule, hence all of these compounds can be used as orally active agents. The chemical structures of 2-mercaptobenzimidazole derivatives were confirmed by FTIR, 1HNMR and 13CNMR spectroscopic data. Molecular docking studies were carried out to predict the binding affinities and interactions of the synthesized compounds with target proteins CA-II (PDB ID: 1A42), and H+ /K+ -ATPase (PDB ID: 5YLU). These derivatives were screened for In-vitro antioxidant potential (DPPH), CA-II, ex-vivo H+ /K+ ATPase assay and in-vivo ethanol-induced gastric ulcer in rats among these M3e, M3i and M3m showed promising results (IC50 = 17.76 μM, 20.73 μM and 30.69 μM), M3e and M3m showed significant results (IC50 = 41.49 μM and 27 μM), M3i and M3m showed enhanced activity 38.82± 3 and 42.45± 2.52. The compound M3e, M3i, M3m exhibited maximum anti-ulcer activity and reduced the ulcer region by, 68 ± 3%, 74 ± 5%, 81 ± 5% respectively. The results obtained from molecular docking studies of synthesized compounds were also in conjunction with their in-vitro, in-vivo and ex-vivo pharmacological activities. Results support

that compounds M3e, M3i and M3m have potent anti-ulcer and antioxidant activities.

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Assessment of Knowledge and Practice of General Public about Disposal of Expired Medicines at Home in Twin Cities of Pakistan

A. Zafar[1], S. Hafeez[1], K. Shaheen[1], M. Irfan[1], R. Khan[1], I. M. Almas[1], and A. Riaz[1]
[1] Hamdard University Islamabad campus, Islamabad, Pakistan.

Article Info

Keywords:
Disposal Practices,
Expired Medicines,
Unused Drugs.

Abstract

The increasing disease burden and lack of adherence of prescribers to standard treatment guidelines in Pakistan has caused higher utilization of medicines at home. The casual attitude of people towards completion of treatment plan increases number of medicines left unused at home and is causing financial as well as malpractice issues regarding handling of medicines at home. The aim of the present study was to assess knowledge and practice of people regarding disposal of expired and unused medicines in twin cities of Pakistan. A descriptive cross-sectional study design was used. A semi-structured questionnaire was developed after extensive literature review and distributed to a sample size of 500 calculated by using Raosoft and selected by convenience sampling. After data collection, data was coded and analyzed statistically. The study revealed that 54% of people visited their physician 3-4 times in last 3 months, 25% visited 5-6 times, 11% visited 7-8 times and 6% visited 8 times. At home, 26% of persons had 6–10, 9% had 0–5, 20% had 11–15 unused medicines, 13% had 16-20 medicines and 3% had 20 medicines at home. 40% people had prescribed and 38% had non-prescribed medicines at home. 60% of respondents had little interest in safe disposal education, 13% were open to it, and 10% thought it was not necessary. 23.5% of people disposed medicines through trash bin, 17% flushed, 8% dumped in soil, 4% return to pharmacy, and 21% donate to others. The study concludes that the general population of twin cities lacks awareness about the disposal techniques for medicines and unfortunately proper disposal of medicines is not considered a serious issue by the general public.

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Assessment of Knowledge and Practice of Women About Use of Cosmetics During Pregnancy in Twin Cities of Pakistan

A. Zafar[1], K. Shaheen[1], S. Hafeez[1], Yusma[1], Samiulah[1], I. Azba[1], and A. Younas[1]
[1] Hamdard University Islamabad campus, Islamabad, Pakistan.

Article Info

Keywords:
Pregnancy Safe Cosmetics, Birth Defects, Awareness.

Abstract

Cosmetics utilization by the females has increased due to raising level of self-grooming and availability of consumer-friendly packages of cosmetics, at the same time the safety of cosmetic products has become a question during pregnancy as cases of birth defects have been reported due to use of particular cosmetic products during pregnancy. The objective of the present study was to assess knowledge and practice of females regarding use of cosmetics during pregnancy and their impact on birth defects. A descriptive cross-sectional study design was used. A semi-structured questionnaire was developed after extensive literature review and distributed to a sample size of 500 females calculated by using Raosoft and selected by convenience sampling. After data collection, data was coded and analyzed statistically. Out of total respondents 60% had gone through more than one pregnancy and 30% had gone through it for once and 10% had gone through it more than once. 30% had no idea about the concept of pregnancy safe cosmetics, 25% had changed their routine about cosmetics use and 45% reported that it has no impact on the baby. 33% reported counseling about safety of cosmetics by the healthcare professionals and 64% had no such session. The study concludes that females in twin cities of Pakistan have lesser awareness about impact of cosmetics and fewer populations have knowledge about availability of pregnancy safe cosmetics.

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Surface Modification of Nano- and Micro Particles with Proteolytic Enzymes for Enhanced Mucosal Drug Delivery

A. Mahmood[1]

[1]College of Pharmacy, Al Ain University, Abu Dhabi campus, Abu Dhabi, UAE

Article Info

Keywords:
Proteolytic Enzymes,
Mucosal Drug Delivery
Nano, Micro Particles.

Abstract

This project was aimed at exploring the ability of proteolytic enzymes (e.g., papain) decorated over the surface of nano-and micro particulate delivery systems in enhancing the mucosal penetration. Mucosal lining is considered as a natural barrier to absorption of drugs, extending over different surfaces such as nasal, ocular, rectal, vaginal and in particular the gastro-intestinal tract (GIT). In order to have a sufficient bioavailability through GI route of administration, after being dissolved a significant amount of drug must permeate the mucosal barrier. A quick look on the biopharmaceutical classification system (BCS) signifies that drugs belonging to BCS class III and class IV have poor permeation across these membranes and therefore, require novel approaches to have enhanced oral bioavailability. Proteases such as papain, bromelain and trypsin can be covalently attached to a suitable carboxylic acid containing moiety via amide bond formation. Nano carriers comprising these conjugates are initially characterized for their size, surface charge, morphology, enzyme activity and drug loading. Afterwards, these carriers are evaluated in-vitro regarding mucus penetration potential and mucus permeation on freshly collected intestinal mucus and intact intestinal mucosa. Initially, promising results have been demonstrated in nano emulsified carriers with mean diameter ranging around 110-150 nm and surface charge between −7 to −0.5 mV. In comparison to control/unmodified carriers, proteolytic enzyme decorated nano-emulsions illustrate a controlled drug release, a higher mucosal permeation and a higher extent of mucus diffusion analyzed in silicon tube assay for enzyme modified carriers. Moreover, high degree of mucosal retention was observed during in-vitro evaluation on rabbit intact mucosa. Overcoming the mucus barrier and delivery of drug at absorption epithelial lining via proteolytic enzyme decorated nano-carriers seems a promising strategy for mucosal drug delivery and enhancing the oral bioavailability of drugs.

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Phytochemical Analysis and Mechanistic Pharmacological Evidence for the Traditional use of Mentha arvensis in Gut Motility Disorders and Gastric ulcer

I. Ullah[1], M. Khan[2], A. Khan[3], and F. Ud Din[4]

[1]Department of Pharmacy, University of Poonch Rawalakot, Pakistan

[2]Department of Pharmacy, Malakand University, Chakdara, Pakistan

[3]Ripha Institute of Pharmaceutical Sciences, Riphah International University, Islamabad, Pakistan

[4]Department of Pharmacy, Quaid e Azam University, Islamabad, Pakistan

Article Info

Keywords:
Mentha arvensis,
Antidiarrheal,
Antisecretory,
Antispasmodic,
Antiulcer.

Abstract

To explore the pharmacological basis for folkloric use of Mentha arvensis for treating gastrointestinal spasm and diarrhea. Mentha arvensis crude extract (Ma.Cr) and four fraction of this plant i.e., aqueous (Ma.Aq), n-hexan (Ma.nH), chloroform (Ma.Ch) and ethyl acetate (Mr.Et) were investigated for phytochemical and GIT motility modification through in-vitro and in-vivo experiments. Isolated rabbit jejunum tissues were employed for in-vitro experiments of antispasmodic activity using power Lab 4/25 data acquisition system. Role of calcium channels was also determined in antispasmodic potential of Mentha arvensis. For antidiarrheal activity (300 and 1000 mg/kg) was investigated in terms of reduction in diarrhea droppings in castor-oil induced diarrhea, while antisecretory activity (300 and 1000 mg/kg) was studied in castor-oil induced model in mice. For antiulcer assay, ethanol-induced gastrointestinal ulcer rat model was used. Mentha arvensis tested positive for flavonoids, tannins and terpenoids. In isolated tissue (rabbit jejunum), Mentha roleana concentration-dependently (0.01 - 3.0 mg/mL) produced relaxation of spontaneous and K+ (80 mM)-induced contractions. Rightward shift of calcium curve confirmed the role of calcium channels in antispasmodic potential of Mentha arvensis. It exhibited protective effect against castor oil-induced diarrhea and intestinal fluid accumulation in mice at 300 - 1000 mg/kg, similar to the standard drugs, loperamide and atropine respectively. Mentha arvensis significantly inhibited ($p < 0.001$) ethanol-induced gastric ulceration in rats. In acute toxicity testing Mentha arvensis did not produce any mortality up to 10 g/kg dose. These results show that Mentha arvensis possesses anti-diarrheal, anti-secretory, antispasmodic and anti-ulcer activities, probably mediated through Ca2+ influx. The presence of phytochemicals, such as flavonoids and tannins, suggest the validity of the acclaimed ethnomedicinal effects in hyperactive gut disorders.

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Antimicrobial Effect and Synergistic Potential of Various Indigenous Plants Against Both Methicillin Sensitive and Resistant Staphylococcus Aureus Strains

A. Hussain[1], S. U. Rehman[1], and I. Ullah[1]
[1]Department of Pharmacy, University of Poonch, Rawalakot, Pakistan

Article Info

Keywords:
Antimicrobial, Oxacillin Resistant *S. aureus*, Bacterial Resistance, Herbal Extracts, Resistance Modifying Plants.

Abstract

Current years have been witnessed that there is an increase of interest in the antibiotic discovery from medicinal plants due to severe side effects, less efficacy or resistance to the existing conventional antibiotics. The aim of this study was to investigate 28 medicinal plants for their activity against ORSA and their resistance modifying effect along with conventional antibiotics. Antimicrobial activity was determined against Oxacillin sensitive (OSSA) and resistant S. aureus strains by using disc diffusion method. Antimicrobial activity was confirmed by determining the MIC and MBC values. Very potent antimicrobial activity was observed in ethanolic extracts from *Camellia sinensis*, *Rosemarinus officinalis*, *Vernonia anthelmintica*, *Ziziphus mauritiana* and Lagerstroemia speciosa with zones of inhibition ranging between 15 mm to 24 mm. nhexane extract of *Eugenia caryophyllata*, chloroform and ethanol fractions of Glycyrrhiza glabra, chloroform fraction of Nigella sativa, ethanol fractions of *Ocimum tenuiflorum* and Oregano vulgare also showed noticeable antimicrobial activity. Few plant extracts showed good potential to increase the antimicrobial effect of β-lactam antibiotics against ORSA. These results can guide the researchers for selection of some plants for further pharmacological investigation and isolation of active constituents.

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Pharmaceutical Industry 4.0 Management Based on Digital Technology: Intelligent Medicine

K. Shoukat[1], M. Jian[1], M. Noreen[2], A. Hussain[3], M. W. Akbar[3], and M. U. Shoukat[4]

[1]School of Management, Wuhan University of Technology, Wuhan, China

[2]Department of Zoology, The Govt. Sadiq College Women University, Bahawalpur, Pakistan

[3]School of Engineering, Bohai University, Jinzhou, China

[4]School of Automotive Engineering, Wuhan University of Technology, Wuhan, China

Article Info

Keywords:
Pharmaceutical Industry 4.0, Management, Digital Technology, Big Data, Intelligent Medicine.

Abstract

With the launch of new strategies such as "German Industry 4.0" and "Made in China 2025", more and more pharmaceutical enterprises have considered the importance of automation and informatization. The adoption of Internet technology, such as internet of things, data science, cloud computing, etc., to realize intelligent production will be the inevitable development trend of pharmaceutical enterprises. Focusing on the current situation of automation, digitalization, information and intelligence in the pharmaceutical industry, and combining with the "Pharmaceutical Industry Development Planning Guide", this paper introduces the driving force, planning scheme and implementation measures of the pharmaceutical industry 4.0. We also discuss the realization path of the value creation of digital technology, and clarifies the important objectives of the smart industry 4.0 at the current stage. Results show that the pharmaceutical industry should focus on the improvement of compliance Intelligent manufacturing engineering projects such as improving production management capacity.

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Classification of X-Ray Images of Pneumonia Using Deep Transfer Learning

M. U. U. Rehman[1], M. Khalid[1], A. Ejaz[2], S. Mujtaba[3], and K. Waris[4]

[1]Department of Computer Science, HITEC University, Taxila.

[2]Department of Computer Science, Capital University of Science and Technology, Islamabad, Pakistan.

[3]Islamabad College for Boys, G-15 Islamabad, Pakistan.

[4]Lahore School of Nursing, The University of Lahore, Lahore, Pakistan.

Article Info

Keywords:
X-Ray,
Pneumonia,
Deep Transfer Learning,
False Negative,
Medical Imaging.

Abstract

Pneumonia is a serious and common respiratory problem that has affected millions of populations worldwide and its patients are likely to be increasing linearly per annum. Pneumonia is a transferable disease that is inflammation and fluid in lungs. The most common tool for prognosis of pneumonia is using chest x-ray imaging modality. Generally, a classification of pneumonia x-ray images is performed manually which requires significant time and effort. Therefore, timing and accurate diagnosis is critical in clinical process. This process can be enhanced using deep transfer learning-based enhancement technique. Deep transfer learning is an efficient and effective technique that has proven its significance in medical diagnosis. Previously, deep transfer learning-based methods have reported promising results in prognosis of pneumonia. This study aims to address this concern of accuracy. In this study, we aim to develop a deep transfer learning model for pneumonia x-ray image classification, using pre-trained models such as ResNet-50, Vgg16, and Xception, and evaluate its performance on a publicly available dataset. To execute the intended work, the authors have selected a pneumonia x-ray images dataset which comprises over 3000+ normal and pneumonia x-ray images. The evaluation was performed on the testing dataset on the basis of higher precision, recall, f-measure, accuracy, sensitivity and specificity scores. According to the study results, the methodology used has achieved higher accuracy of 95.95% with a lower false negative rate of 2.1%. We conclude that this ResNet-50 deep transfer learning-based methodology is a robust approach as compared with Xception and Vgg16 models because it has provided higher accuracy and reported a lower number of errors during the simulation and model training. Now it is capable enough to classify pneumonia x-ray images effectively. The findings of this study could have significant implications for improving the accuracy and efficiency of pneumonia diagnosis, and for developing deep learning models for other medical imaging applications.

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Evaluation of the Antimicrobial Synergistic Potential of Fagonia indica Burm. F. With the Selected Antibiotic

A. Abrar[1], H. Ahmed[1], H. Fatima[1], K. Bilal[1], S. A. Mohsin[1], D. Waseem[2], and I. Ul Haq[1]

[1]Department of Pharmacy, Faculty of Biological Sciences, Quaid-i-Azam University, Islamabad, Pakistan

[2]Shifa College of Pharmaceutical Sciences, Shifa Tameer-e-Millat University, Islamabad, Pakistan

Article Info

Keywords:
Fagonia indica, Synergistic Potential, Antimicrobial, Scanning Electron Microscopy.

Abstract

Antimicrobial resistance is the predominant side effect of human antibiotic abuse and overuse. Literature evident that Fagonia indica Burm.f. has well developed ethnomedicinal antimicrobial profile for treatment of multiple infections. The present study aims to determine F. indica antimicrobial synergistic effect with a selected antibiotic against resistant bacterial isolates. The phytochemical quantification was performed by total phenolic content (TPC), total flavonoid content (TFC), and reverse phase-High Pressure Liquid Chromatography (RP-HPLC) of F. indica four extracts (n-hexane (n-Hex), ethyl acetate (E.A), methanol (MeOH), and aqueous (Aq.)). The preliminary resistant profiling of selected antibiotics against resistant gram-positive (Staphylococcus haemolyticus and MRSA) and gram-negative bacteria (Escherichia coli and Pseudomonas aeruginosa) was evaluated. The antimicrobial potential then the synergistic potential of extracts was assessed against selected isolates. Furthermore, the time-kill kinetics and protein content quantification were also performed. Scanning electron microscopy was conducted to evaluate the synergistic effect topographically. The phytochemical screening showed that MeOH extract had maximum phenolic (28.4±0.67 µg GAE/mg) and flavanoid content (11±0.42 µg QE/mg). The RP-HPLC results displayed maximum polyphenols (12.372 ± 0.01 µg/mg) in MeOH extract. Prelimnary resistant profiling shows selected clinical isolates were resistant to Cefixime. All extracts showed substantial antibacterial potential except Aq. extract with MIC ranges from 150-300 µg/ml. The n-Hex showed the synergistic potential against R.E. coli and R. P. aeruginosa while MeOH extract against MRSA and R.S. haemolyticus with a four-fold reduction in cefixime dose respectively. The time-kill kinetic studies revealed that almost all extracts in synergy inhibited the growth of bacteria from 3 to 12 hour. The percentage protein inhibition was maximum with extracts in combination illustrating its mechanism could be at multiple sites. SEM images displayed bacterial cell disruption at synergistic concentrations. It is concluded that F. indica extracts can potentially reduce antimicrobial resistance against cefixime and can be investigated further for in-depth mechanistic and in vivo studies.

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In-sillico Pharmacokinetic Assessment of Fast Release Tablets of Domperidone and its Comparison with Conventional Tablets

B. Alam[1], S. Nazir[1], and A. Khan [1]
[1]Department of Pharmacy, Kohat University of Science and Technology, Kohat, Pakistan

Article Info

Keywords:
Domperidone,
Dispersible Tablets,
Effervescent Tablets,
Pharmacokinetics,
BCS Class II.

Abstract

Domperidone is a BCS Class II drug that has been used for the management of GERD as an add-on treatment in adults and children. As precision of dosing and patient's compliance become important prerequisite for quick relief from emesis, there is a need to develop a formulation for this drug which overcomes problems such as difficulty in swallowing, inconvenience in administration while traveling and better compliance. Pharmacokinetic studies help to determine bioavailability and to understand in vivo behaviour of drugs which could be further translated to assess therapeutic efficacy and safety profiles. Rrecently FDA has approved the use of Physiology Based Pharmacokinetic Modeling (PBPK) simulations as an alternative to clinical trials for pharmacokinetic assessments. Use of simulation software helps to manage experimental workload, time, and lack of resources required for in-vivo studies. In the current study, effect of formulation variables on pharmacokinetic response was evaluated. The current study was conducted to assess pharmacokinetics of fast release tablets of domperidone (oro dispersible tablets and effervescent tablets) and their comparison with conventional marketed tablets. Both ODTs and effervescent tablets were prepared by direct compression method. All formulations were evaluated for different quality control parameters like physical characteristics (physical appearance, shape, weight, weight variation and thickness), mechanical strength (crushing strength, specific crushing strength, tensile strength and friability), disintegration behavior (in vitro disintegration time, oral disintegration time and effervescence time) assay and in vitro drug release. All the parameters were determined as per official compendia (USP and BP). In silico pharmacokinetics was assessed in Asian and European population, using physiology based pharmacokinetic (PBPK) modeling software platform PK-Sim/MoBi (Bayer Technology Services, Leverkusen, Germany) version 10. An effective, pleasant tasting formulation was found to have a good hardness of 3 kg/cm2, disintegration time of 27±1 seconds and in vitro drug release of not less than 99% within 30 minutes. The drug release from ODTs was studied according to British pharmacopeia, using 900 mL of 0.1 N HCl as dissolution media held at 37 ± 2 oC. Highest C-max was observed with ODTs of domperidone which was 82.26 ± 5.66 ng/ml and was not significantly different from the Cmax of the effervescent tablets and there was a significant difference in Tmax of the conventional tablet and fast dispersible tablets.

Tmax of ODTs, effervescent tablets were 29.56 ± 4.29, 29.99 ± 5.37 and reference tablets was 60 ± 5.67, respectively In comparison with convention pharmacokinetics study in biological subjects, in silico pharmacokinetics is an effective and rapid mean of predicting in vivo behavior of the drug. It is helpful during designing and development of a novel dosage form as the effect of changes in formulation and process variables on pharmacokinetics can be easily studied.

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Making More Sense in Post Market Pharmaceutical Research and Data

N.I. Bukhari[1]

[1] University College of Pharmacy, University of the Punjab, Lahore, Pakistan.

Article Info

Keywords:
Post Market,
Pharmaceutical Research,
In-Vitro,
In-Vivo,
Ex-Vivo,
In-Silico,
Correlation.

Abstract

The dosage forms are continuously improved after their marketing and the role of the post market research for improving an existing formulation is well established. The time line, output reliability and interpretation for such research are critical. Though, the use of artificial intelligence has been empathised by the regulatory authorities, yet the multiple formulations are prepared using the conventional time-taking and expensive approach. Literature reviews need to establish the novelty of the work. In-vitro and in-vivo studies are carried out but without their correlations. The issues of the data paucity and deluge have usually been noted. In transdermal delivery systems, flux is not reported. Indeed, after economical formulation optimization with computer-aided approaches, the time, number of studies and animals/human could be reduced by an appropriate planning – in-vitro, in-vivo, ex-vivo, in-silico and real-time in-vivo studies. Establishing a correlation between the appropriate pairs of above characterizations, such as between in-vitro dissolution and absorption data could offer more insight and data reusability by other researchers. Thus, time line, output reliability and interpretation of research outputs could tremendously be improved with putting lesser efforts.

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7,8-Dihydroxyflavone A Trkb Agonist Alleviated Diabetically Induced Cognitive Impairment, Conversing Both Behavioral and Neurochemical Correlates in the Frontal Cortex, Hippocampus and Striatum

M.Arif[1], K. Rauf [1], N. U. Rehman[2], A. Tokhi[1], Z. Ahmed[1], M. S. Khan[3], H. Malik[1], and R. D. Sewell[4]

[1]Department of Pharmacy, Comsats University Islamabad, Abbottabad Campus, Pakistan
[2]Department of Pharmacy, Gomal University, Dera Ismail Khan, Pakistan
[3]Head of the Pharmacy Services Department, Ayub Teaching Hospital Abbottabad, Pakistan
[4]Cardiff School of Pharmacy and Pharmaceutical Sciences, Cardiff University, Cardiff, UK

Article Info

Keywords:
7,8-DHF,
Flavone,
Diabetes,
Cognition,
Catecholamines,
Vitamin C.

Abstract

Cognitive decline in diabetes is a hallmark of the series of pathologies within the brain that are primarily secondary to persistent hyperglycemia, advanced glycation end products, cholinergic dysfunction and oxidative stress, impaired insulin signaling and cerebrovascular changes. A flavonoid, 7,8-dihydroxyflavone (7,8-DHF) has documented anti-inflammatory and antioxidant effects, which are thought to be the main determinants in slowing cognitive decline. Male BALB/c mice were given a single 200 mg/kg i.p. injection of streptozotocin (STZ) on protocol day 1; 21 days later, once the presence of diabetes had been confirmed, the animals were given either donepezil (4 mg/kg) or 7,8-DHF (5–15 mg/kg). Multiple behavioral paradigms, including the open field test, the Y-maze, new object recognition, socializing, Morris water maze, nest-building behavior and the open field were used to examine the cognitive impairment brought on by diabetes. Following behavioral evaluation, HPLC with UV detection was used to measure postmortem adenosine and its metabolites as well as dopamine, serotonin, noradrenaline and vitamin C in the hippocampus, frontal cortex, and striatum. These behavioral shortfalls were partially restored by higher doses of 7,8-DHF in most of the cases as well as frontal cortical, hippocampal and striatal noradrenaline, serotonin, and Vitamin C levels were restored. The present study delivers a worthy possibility to study additional aspects of 7,8-DHF in diabetes-induced cognitive decline.7,8-DHF significantly improved multiple parameters of diabetes cognitive decline in behavioral studies along with a significant upsurge of dopamine, serotonin, noradrenaline and vitamin C in fundamental brain sections involved in learning and memory. Adenosine and its metabolized were also significantly lowered to impart neuroprotection.

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Inhibitory Effects of Berberis lycium and Its Major Constituent Berberine on Inflammation Associated Corneal Neovascularization

S. L. Shah[1], F. Wahid[2], J. U. Rahman[1], Z. Ahmed[1], A. J. Shah[1], and T. Khan[1]

[1] Department of Pharmacy, Comsats University Islamabad, Abbottabad Campus, Abbottabad, Pakistan

[2] Department of Biomedical Sciences, Pak-Austria Fachhochschule: Institute of Applied Sciences and Technology, Haripur, Pakistan

Article Info

Keywords:
Berberis lycium,
Berberine,
Corneal Neovascularization,
Histopathology,
TLC,
HPLC.

Abstract

Berberis lycium Royle belongs to the berberidaceae family. It is traditionally used for the treatment of ophthalmic disorders but never been investigated for corneal neovascularization (CNV). The present study aimed to evaluate the phytochemical constituents and to investigate the pharmacological potential of B. lycium extract (Bl.Cr) and its major constituent berberine in CNV. For this purpose, B. lycium roots were macerated with methanol for 21,7 and 3 days. The Bl.Cr was phytochemically investigated for detection of flavonoids, alkaloids, phenol, carbohydrates, phyto-sterols, saponins, tannins, proteins and glycosides using standard chemical tests. Thin layer chromatography (TLC) was performed for the detection of berberine, a major constituent of B. lycium. For the analysis of plant extract and berberine, high performance liquid chromatography (HPLC) was used. For CNV, rabbits were divided into four groups and CNV was induced by the alkali burn (1N NaOH) method. Topical treatment was started with Bl.Cr, berberine, and dexamethasone after 7 days and continued for the next 21 days (3 drops thrice daily). The CNV was evaluated through photographic analysis and histological studies. Phytochemical analysis of Bl.Cr showed the presence of alkaloids, flavonoids, saponins, phenols, and carbohydrates. TLC and HPLC methods confirmed the presence of berberine in Bl.Cr. Photographic analysis of Bl.Cr and berberine-treated groups exhibited a remarkable decrease in CNV. The histological results of Bl.Cr and berberine-treated groups also presented no blood vessels with properly arranged collagen fibers. Based on these results, it is concluded that B. lycium as well as berberine may have positive prospects for the treatment of CNV.

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Development of a Nano-loaded Transdermal Patch for Diabetic Wound Healing

Adeel. M.Butt[1], N. Abdullah[2], A. Sattar[1], and S. Maqsood[1]

[1]Institute of Pharmaceutical Sciences, University of Veterinary and Animal Sciences, Lahore, Pakistan

[2]Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan

Article Info

Keywords:
Metformin,
Silver Nanoparticles,
Diabetic Wound Healing,
TDDS Patch.

Abstract

We formulated and characterized a TDDS patch containing metformin loaded silver nanoparticles. Firstly, silver nanoparticles were prepared as follows. Aqueous solutions of sodium borohydride and trisdium citrate were prepared, mixed and heated for 30 minutes in dark at 60°C under continuous magnetic stirring. Subsequently, the prepared silver nitrate solution and metformin solution at similar concentrations, prepared beforehand, were introduced in the mixture drop by drop. Change in color from transparent to yellow indicated the formation of silver nanoparticles. The solution was further heated at 80-85°C for 20 minutes to complete the preparation of silver nanoparticles loaded with metformin. TDDS was prepared by solvent evaporation method. Briefly, 5% PVA solution was prepared by mixing it in distilled water for 2 hours. Different concentrations of PVP solution were prepared by dissolving it in distilled water. Then, PVA and PVP solutions were mixed by magnetic stirring for 30 minutes to form a homogenous solution. PEG 400 was added as a plasticizer and glycerin was also added to make the peeling of films easier. The prepared nanoparticles suspension was added to the above mixture and stirred for 5 minutes followed by pouring in pre-dried petri dishes. The mixtures were kept in oven for drying for 48 hours. Dried patches were then peeled and kept in desiccator by wrapping in aluminum foil. Entrapment efficiency of the optimized metformin silver nanoparticles formulation was 75.27%, particles size showed variation between 100 to 300 nm, with optimized formulation showing average size of 250 nm. FTIR and SEM analysis confirmed the development of stable nanoparticles and there was no interaction of excipients with drugs. Moisture content, moisture uptake, and water vapour transmission rates of the prepared formulation were 6.74 to 8.02%, 11.39 to 13.45%, 0.09 to 0.10% respectively. We suggest that the prepared TDDS patches containing metformin loaded silver nanoparticles could help in diabetic wound healing.

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Dissecting Tumor Immune Microenvironment in Hospitalized Cancer Patients

S. Afridi[1,2,4], Z. Wu[1], G. Song[2], M. Zhang[2], S. Goswami[2], H. Yang[3], and X. Zhang[2]

[1]Department of Pediatric Intensive Care Unit, Guangzhou Institute of Pediatrics, Guangzhou Women and Children's Medical Center, Joint Center for Infection and Immunity, Guangzhou Medical University, Guangzhou, China

[2]The Center for Microbes, Development, and Health, Key Laboratory of Molecular Virology and Immunology, Institute Pasteur of Shanghai, Chinese Academy of Sciences, Shanghai, China

[3]Department of Gynecological Oncology, Shanghai Cancer Center, Fudan University, Shanghai, China

[4]Department of Allied Health Sciences, Faculty of Life Sciences, Sarhad University of Science & Information Technology Mardan Campus, Mardan, Pakistan

Article Info

Keywords:
Cancer,
Cervical Squamous Cell Carcinoma,
Biomarker,
HLADRhi.

Abstract

Cancer is one of the top ten leading causes of death worldwide. For prognostic assessments and therapeutic choices, correct disease staging must be determined. Although many different approaches have been tried so far, more research is still needed to fully understand the intricate interactions between tumors and the environment that supports them. Herein, we dichotomized the Tumor Immune Microenvironment in hospitalized Cancer Patients using standard techniques including FACS, 10X Genomics, and mFIHC analysis. To assess the plasticity and phenotypes of immune cells within the Tumor Immune microenvironment we identified distinct immune cell populations in different cancer types. First, we recognized that the HLADRhi Treg significantly increased in cervical squamous cell carcinoma (CSCC) patients compared to healthy donors. Quantitative multiplexed immunohistochemistry revealed that an increase in the number of tumors infiltrating HLADRhi Tregs is associated with unfavorable classical risk parameters of advanced disease stage and stromal invasion. In the current study, we identify and characterize unique populations of highly activated and immunosuppressive HLADRhi Tregs. An increased HLADRhi Treg frequency may be a potential biomarker to stratify patients and to evaluate therapeutic efficacies in personalized immuno-oncology studies.

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7,8-Dihydroxyflavone Reverses Chronic Ethanol Induced Cognitive Impairment by Restoring Catecholamine Levels in the Brain

M. Arif[1], K. Rauf[1], N. U. Rehman[2], H. Malik[1], M. S. Khan[3], Z. Ahmed[1], N. Nawaz[4], and R. D. Sewell[5]

[1]Department of Pharmacy, Comsats University Islamabad, Abbottabad Campus, Pakistan

[2]Department of Pharmacy, Gomal University, Dera Ismail Khan, Pakistan

[3]Head of the Pharmacy Services Department, Ayub Teaching Hospital, Abbottabad, Pakistan

[4]Department of Pharmacy, City University of Science and Information Technology, Peshawar, Pakistan

[5]Cardiff School of Pharmacy and Pharmaceutical Sciences, Cardiff University, Cardiff, UK

Article Info

Keywords:
7,8-DHF,
Chronic Ethanol Induce Cognitive Impairment,
Vitamin C,
Augmented amyloid-β (Aβ),
Tau levels,
Dopamine.

Abstract

An imperative loss of cognition is caused by neuroinflammation and neurodegeneration caused by chronic drinking. The TrkB agonist 7,8-dihydroxyflavone (7,8-DHF) reverses the effects of diabetes and a high-fat diet on the cognitive function of rats. Dopamine, noradrenaline, and vitamin C levels were not examined to determine their effects on these three substances. For 24 consecutive days, 4 mg/kg of donepezil and 5, 10, and 15 mg/kg 7,8-DHF were administered to selected groups of male mice. After 24 days of treatment, ethanol treatment was stopped for 6 days. Using the Morris water maze, locomotion, socializing, nest-building behavior, Y-maze, and novel object recognition. The animals were assessed for cognitive skills on different days (1, 12,24, during abstinence (day 26), and on the seventh day of the washout period. Ultimately, the animals were killed, and the amounts of vitamin C, dopamine (DA), noradrenaline (NA), adenosine, and its metabolites were measured in key brain areas using HPLC-UV. Analysis of the data revealed that 7,8-DHF considerably reduced ethanol withdrawal-induced hypo-locomotion and improved exploratory behavior in the Y-maze, novel object, and MWM. Significant improvements have also been made in socialization and nest-building activities. Augmentation of DA and NA in the frontal cortex, vitamin C in the hippocampus, and dopamine in the striatum was observed by 7,8-DHF after HPLC quantification. The upsurge in adenosine and its metabolites was also significantly repressed in key brain areas. In conclusion, the special effect of chronic ethanol on cognitive decline was reduced by 7,8-DHF and donepezil, which also reestablished critical neurotransmitter levels in regions of the brain important for cognition and memory combined with vitamin C.

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Phytochemical Screening, Anti-oxidant and Anti-cancer Potential of Otostegia limbata Extract on Breast Cancer Cells

J. U. Rahman[1], M. Ikram[1], H. M. Rasheed[1], S. L. Shah[1], F. Wahid[2], and T. Khan[1]

[1]Department of Pharmacy, Comsats University Islamabad, Abbottabad, Pakistan

[2]Department of Biotechnology, Comsats University Islamabad, Abbottabad, Pakistan

[2]Department of Biomedical Sciences, Pak-Austria Fachhochschule: Institute of Applied Sciences and Technology, Haripur, Pakistan

Article Info

Keywords:
Otostegia Limbata,
Breast Cancer,
MCF-7 Breast Cancer Cell Lines.

Abstract

Traditionally, O. limbata is used for the treatment of various diseases including cancer. However, literature lacks scientific investigation on this plant in breast cancer activity. The present study was aimed to evaluate the major phytoconstituents, total flavonoids and total phenolic contents, anti-oxidant and anti-breast cancer potential of plant crude extract and its fractions. Aerial parts of O. limbata were collected and subjected to extraction with methanol using solvents with increasing order of polarity. Phytochemical investigation of O. limbata crude extract was performed using various chemical tests. Total phenolic and flavonoids contents of plant crude extract and its fraction were estimated by Folin-Coicalteu and colorimetric methods, respectively. Anti-oxidant activity of the crude extract and their fractions were performed using DPPH free radical scavenging assay. Anti-cancer effect of crude extract and their fractions were assessed by WST-8 assay against MCF-7 breast cancer cell lines. The preliminary phytochemicals tests showed that the plant extract contained various classes of chemical compounds such as tannins, alkaloids, flavonoid, phenols, carbohydrates, saponins and terpenoids. O. limbata crude extract and fractions exhibited good DPPH scavenging activity in which ethyl acetate and n-butanol fraction showed highest anti-oxidant potential (90.34±0.22 and 89.06±0.26%) even greater than the standard ascorbic acid (80.18±1.77%). The crude extract was found to be safe against normal fibroblast (NIH-3T3) cells (75.09%) at maximum dose of 250 µg/mL. Whereas, n-hexane and chloroform fractions showed remarkable reduction in the cell viability (20.95±0.45 and 51.10±15.15) of breast cancer (MCF-7) cells at 250 µg/mL dose. These data showed that O. limbata crude extract and fractions, n-hexane and chloroform, significantly reduced the viability in cancer cells and have high potential as anticancer agents.

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Role of Biosynthetic Silver Nanoparticles in Inhibition of the Malignant Behavior of Gastric Cancer Cells and Enhancement the Therapeutic Effect of 5-Fluorouracil

J. Yuan[1], S. U. Khan [2], J. Luo[1], Y. Jiang [1], Y. Yang [1], J. Yan [1], and Q. Tong [1]
[1]Department of Gastrointestinal Surgery I Section, Renmin Hospital of Wuhan University, Wuhan, 430060, China

Article Info

Keywords:
Gastric Cancer,
Biosynthetic Nano Silver,
Chemically Synthesized Nano Silver,
5-Fluorouracil,
Apoptosis,
ROS.

Abstract

Gastric cancer (GC) is the fourth leading cause of cancer death worldwide. Silver nanoparticles are increasingly used in the diagnosis and treatment of cancer due to their cytocompatibility, drug delivery, and cell targeting. This study investigated the role of biosynthetic silver nanoparticles in the development and 5-Fluorouracil (5F) drug resistance of GC. CCK8 was used to detect cell survival rate. Colony formation assay and Transwell assay were performed to confirm cell growth, migration, and invasion ability. RT-PCR was used to detect mRNA expression levels of genes. DCF-DA and DHE fluorescent probes were used to detect intracellular ROS expression. Biosynthetic silver nanoparticles had a better killing effect on GC than chemosynthetic silver nanoparticles. When combined with 5F, biosynthetic silver nanoparticles had a better inhibition effect on proliferation, migration, and invasion of GC. When used alone or in combination with 5F, biosynthesized silver nanoparticles can increase Bax and p53 and decrease Bcl2 expression. Biological silver nanoparticles increased intracellular ROS, especially when combined with 5F. Biosynthetic silver nanoparticles inhibit and enhance 5F to inhibit the growth, migration, and invasion of GC cells by promoting apoptosis and increasing intracellular ROS.

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Reducing the Threshold of Primary Prevention of Cardiovascular Disease to 10% Over 10 Years: The Implications of Altered Intensity 'Statin' Therapy Guidance

S. Sultan[1], S. U. Khan[2,3], K. Holden[1], A. A. Hendi, A. Abbas[5], U. Zaman[6], S. Naeem[7], K. Rehman[6]

[1]Faculty of Health Sciences and Wellbeing, University of Sunderland, UK.

[2]Department of Biochemistry, Women Medical and Dental College, Khyber Medical University Khyber Pakhtunkhwa, Pakistan

[3]National Key Laboratory of Crops Genetic Improvement, Huazhong Agricultural University, Wuhan, P. R. 430070, China.

[4]Department of Physics, College of Science, Princesses Nourah bint Abdulrahman University, P.O. Box 84428, Riyadh 11671, Saudi Arabia

[5]Peshawar Institute of Cardiology, Peshawar, KPK, Pakistan.

[6]Institute of Chemical Sciences, Gomal University, Dera Ismail, Khan, KPK, Pakistan.

[7]Department of Pharmacy, Faculty of Medical and Health Sciences, University of Poonch Rawalakot.

Article Info

Keywords:
Statins,
CVD reduction,
randomized controlled trials.

Abstract

Cardiovascular disease (CVD) is a significant non-communicable disease associated with high long-term mortality. In addition to more effective secondary therapies, the primary prevention of CVD has developed markedly in the past several years. This study aims to investigate the evidence and impact of reducing the threshold for primary CVD risk management to 10% over 10 years with 'statin' therapy. To conduct research a systematic review utilizing five electronic database searches was completed for studies, analyzing the clinical effect of reducing the threshold of CVD risk to 10% over 10 years for primary prevention with statin therapy. The study included six (6) trials. Statin therapy was allocated to 31018 participants. The mean age was 61 years and the mean follow-up was 4.6 years. The mean relative reduction in total cholesterol was 19% (from an average of), low-density lipoprotein cholesterol was 28.3% (from mmol/L to mmol/L) and triglycerides were 14.8% (from mmol/L to mmol/L). High-density lipoprotein cholesterol was observed to increase by a mean of 3.3% (from mmol/L to mmol/L). When examining all-cause mortality, statin therapy was associated with a 12% relative risk reduction compared with control, where overall rates were reduced from 1.4% to 1. % There is a 30% risk reduction in general major coronary events. There is a 19% risk reduction in general major cerebrovascular events with the statin group. Whilst there is undoubtedly statistical evidence that supports the observation of the effectiveness of statin therapy for primary prevention,

	there is a risk that many hundreds of patients need to be treated to avoid a single adverse clinical outcome.

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Development and Evaluation of the Bioinspired pH-responsive Sericin-Chitosan Based Hydrogels for the Controlled Colonic Delivery of PETase; Harnessing the PETase Triggered Degradation of Microplastics

A. Ullah[1], G. Lee[1], H. Kim[1], H. T. Kwon[1], S. I. Lim[1]
[1]School of Chemical Engineering, Pukyong National University, Busan 48513, Republic of Korea

Article Info

Keywords:
pH-responsive hydrogels,
PETase delivery,
PET Degradation,
Chitosan,
Sericin,
microplastics.

Abstract

The gravity of the microplastic pollution posed impending threats to the environment cannot be overestimated. Being a ubiquitous pollutant in the living environment, the microplastics reach humans through the food chain causing various hazardous effects. The microplastics can be effectively degraded by the PETase enzyme. In the current study, for the first-time hydrogel encapsulated, bioinspired colonic delivery of PETase has been reported. The free radical polymerization-assisted hydrogel system was synthesized from sericin, chitosan, and acrylic acid using MBA as a crosslinker, and ammonium persulfate as an initiator. The hydrogels were characterized through FTIR, PXRD, SEM, and thermal analysis confirming the development of a stabilized hydrogel system. The hydrogel showed 61% encapsulation efficiency, maximum swelling, and cumulative PETase release (96%) at pH 7.4. The mechanism of PETase release exhibits the Higuchi pattern of release with an anomalous transport mechanism. The post-release structural integrity of PETase was confirmed through the SDS-PAGE technique confirming the preserved protein structure. The in-vitro polyethylene terephthalate (PET) degradation activity of the released PETase exhibited the concentration and time-dependent degradation of PET. The developed hydrogel system exhibited the intended features of a stimuli-sensitive carrier system that can be efficiently used for the delivery of PETase to the colon

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LC-MS/MS based GNPS Molecular Networking, Assessment of Antioxidants Capacity and Antiglioma Potential of Clematis graveolens

Z. Ahmed[1], M. Ikram[1], I. Khan[1], K. Bashir[1], A. J. Shah[1], H. Xang[1] and T. Khan[1]
[1]Department of Pharmacy, Comsats University Islamabad, Abbottabad, Pakistan

Article Info

Keywords:
GNPS Molecular Networking, Antioxidants Capacity, Phytochemical, Antiglioma Potential, Cytotoxic potential.

Abstract

Clematis graveolens is a native climber plant in the Himalayan regions. This study investigates the phytochemical composition, antioxidant capacity, and cytotoxic effects of C. graveolens crude extract and its fractions. The total phenolic content of crude extract and its fractions ranged from 43.4 to 338.7 µg GAE/mg of samples whereas total flavonoid contents ranged from 0.92 to 177 µg QE/mg of samples. For ABTS scavenging activity, the ethyl acetate fraction showed significant inhibitory concentration with the IC50 value of 39.50 µg/mL followed by chloroform fraction with the IC50 value of 50.99 µg/mL. For DPPH assay, the most active fraction was ethyl acetate with the IC50 value of 32.27 µg/mL followed by chloroform fraction with the IC50 value of 44.12 µg/mL. In the metal chelation assay it was observed that ethyl acetate fraction has significant IC50 value of 53.46 µg/mL followed by chloroform fraction with the IC50 value of 77.20 µg/mL. The cell cytotoxicity was determined using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide viability assay against U-87 (human glioma cells) and BHK-21 (human normal kidney cells). The crude extract (IC50 = 112.0 µg/mL), the ethyl acetate fraction (IC50 = 138.1 µg/mL), and chloroform fraction (IC50 = 142.7 µg/mL) showed significant inhibitory activity. The nHexane and n-Butanol fraction showed moderate activity with the IC50 value of 167.8 µg/mL and 176.1 µg/mL respectively. Moreover, C. graveolens extract showed negligible toxicity against BHK-21 (human normal kidney cells) at the maximum concentration. Additionally, liquid chromatography coupled with mass spectroscopy was performed to characterize metabolite profiling of Clematis graveolens. The LC-MS/MS data was uploaded to GNPS platform to annotate compounds and their family clusters. Total 714 nodes were annotated with different compound classes. In this study, 27 compounds were identified majority of which were phenolic in nature. This study provides detailed metabolite profiling of Clematis graveolens its antioxidant and cytotoxic potential.

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Microneedles: A Smart Approach for Enhancement of Site-Specific Drug Delivery against Wound Infections

M.Mir[1]
[1]Department of Pharmacy, Iqra University Islamabad Campus, Pakistan

Article Info

Keywords:
Microneedles,
Drug Delivery,
Site-Specific,
Dermatokinetic,
Wound Infections.

Abstract

Management of infected wounds has become a major public health concern, due to increasing prevalence of chronic wounds, escalating antimicrobial resistance and lack of viable methods for delivery of antimicrobials. Carvacrol (CAR) has substantial antimicrobial activity against multidrug resistant pathogens. In current study, CAR was developed into a site-specific nanoparticles (NPs) based delivery system using bacterial lipase sensitive poly(Ɛ-caprolactone) (PCL). The release studies displayed a remarkably higher release of CAR from NPs in the presence of bacterial lipases in contrast to the absence of bacterial enzyme, highlighting their potential for infection responsive delivery. Furthermore, entrapment of CAR in the NPs resulted in a 2-4-fold increase in its antimicrobial potential against both planktonic and biofilm grown Gram-positive and Gram-negative bacteria. Considering the nature of the target site, various dosage forms including hydrogels, dissolving microneedle (MN) arrays and liquid injection systems were investigated as delivery devices. Dermatokinetic studies revealed that in contrast to pure CAR, CAR-PCL NPs remained available at the site of application for a longer time demonstrating the potential of CAR-PCL NPs for both site-specific delivery and sustained antimicrobial effect. All three dosage forms tested, successfully delivered the CAR-PCL NPs to the desired site. However, MN based systems (CAR-PCL NPs-MNs and AdminPen® 1500), delivered >90% of the total applied CAR, in comparison to CAR-PCL NPs loaded hydrogel (15% only) demonstrating the superiority of the MN systems over hydrogel in terms of drug delivery efficiency. Consequently, these findings proved that this advanced drug delivery platform laden with CAR may lead to the desired site-specific antimicrobial effect and could be an effective approach for the potential treatment of infected wounds.

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Combating Cancer: Natural Products and Pseudo Natural Products-based strategies underpinned by Medicinal Chemistry

H. Hussain[1]

[1] Leibniz Institute of Plant Biochemistry, Department of Bioorganic Chemistry, Weinberg 3, D-06120 Halle, Germany

Article Info

Keywords:
Natural product ,
Phytochemical,
Bioactive,
NP-derived derivatives,
Anticancer.

Abstract

It has been reported that natural products (NPs) have an excellent track record in the discovery of lead compounds to treat various human diseases. A characteristic feature of natural products is their chemical diversity, which is created by a sequence of enzymatic reactions in the producing organisms. The phytochemical investigations of plants and fungi provided a continuous supply of the natural products of interest but with limited number of their derivatives. Moreover, synthetic chemists are applying rational approaches to the generation of lead-like libraries to achieve increased potency, broader biological activity and fewer side effects and thus, a number of clinically important NP-derived derivatives have reached the market. We have isolated a number of natural products (viz., triterpenes, polyketides, and phenazines etc) from fungi and plants which have interesting chemical diversity. Following the natural product inspired diversity-oriented synthesis strategy, various derivatives of these bioactive natural products have been prepared with the objective to obtain compounds with greater anticancer effects.

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Engaging Community Pharmacies in Early Detection of Missing Tuberculosis Patients through Public–Private Mix Intervention in Pakistan

Waseem Ullah,[1,2,3] Hadi Almansour,[3] Razia Fatima,[4] Bandana Saini,[3,5] and Gul Majid Khan[1]

[1]Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan

[2]Department of Pharmacy Practice, Shifa College of Pharmaceutical Sciences, Shida Tameer-e-Millat University Islamabad, Pakistan

[3]School of Pharmacy, Faculty of Medicine and Health, University of Sydney, Sydney, Australia

[4]Chief Research Unit, National Tuberculosis Control Program, Islamabad, Pakistan

[5]The Woolcock Institute of Medical Research, Sydney, Australia

Article Info

Keywords:
Implementation Science,
Case Notification,
Pharmaceutical Public Health,
Pharmacy Referral Network,
Case Notification,
Public-Private-Partnership.

Abstract

Globally, Pakistan ranks fifth in terms of missing tuberculosis (TB) patients' burden. Missed TB cases are either undiagnosed or diagnosed but not notified to the national TB database. Public–private mix interventions are contributing significantly to the case detection, diagnosis, and treatment of TB in Pakistan. However, it is estimated that many cases of infected TB patients go undetected. It is likely that these "undiagnosed" active TB cases seek treatment from community pharmacies, among other venues. This study aimed at assessing the feasibility of community pharmacy–based TB case detection. Case detection protocol implementation in three Pakistani districts in a non-random selection of pharmacies was followed by a review of routinely maintained prospective records of patients referred from these private community pharmacies to general practitioner (GP) clinics. The study engaged 500 community pharmacies for referring presumptive TB patients to GP clinics. In total, 85% of the engaged pharmacies remained active in providing referrals during the study period. The community pharmacy–referral network achieved an annual referral rate of 3,025 presumptive TB patients and identified 547 active TB cases for the period January–December 2017. Every fifth referral among presumptives presenting and counseled at pharmacies was diagnosed with TB at GP clinics. This contribution was 9% of all new TB cases identified in these districts through all other private venues linked with the Greenstar Social Marketing setup. Identified barriers and facilitators to implementation and cost effectiveness of pharmacy models for TB case detection should be considered if the model were to be scaled up.

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Crafting of hydroxyapatite embedded gelatin nanoparticles via nanoprecipitation method against Rheumatoid Arthritis

Q. U. Ain[1]
[1] Department of Pharmacy, Quaid-i-Azam University, Islamabad, Pakistan.

Article Info

Keywords:
Rheumatoid arthritis,
Nano-particulate-based drug delivery,
Tofacitinib (Tofa) loaded nanohydroxyapatite (nHA) embedded gelatin (GLT) nanoparticles (NPs).

Abstract

Rheumatoid arthritis (RA) is a chronic autoimmune disease of unknown etiology with much higher prevalence in world's population. RA is initially associated with inflammation of joints and cartilages that ultimately leads to their destruction thus requiring a therapeutic intervention. Bone deformities as one major impact of RA progression potentiates the need for both bone regeneration approach along with the therapeutic treatment of RA. In the past few decades, nano-particulate-based drug delivery approaches that have been investigated for the treatment of RA, include ceramics, polymers, and hydrogels. Among these nanocarrier systems, ceramics like hydroxyapatite have gathered striking attention due to their bioactive, biocompatible, and bio-conductive characteristics. Nano-sized hydroxyapatite (nHA) permeates the bone tissues and serves as a source of calcium phosphates required for bone repairing that are damaged during disease process. Moreover, biopolymers like gelatin have been explored as biopolymer to fabricate a biomimetic nanocarrier system. Therefore, in the current research, gelatin and nHA have been explored as drug nanocarrier with bone supplement potential. Tofacitinib (Tofa) loaded nanohydroxyapatite (nHA) embedded gelatin (GLT) nanoparticles (NPs) (TofanHA-GLT NPs) have been fabricated for targeted drug delivery at an arthritic joint along with bone resorption approach. Quality by Design (QbD) approach was opted to determine the most significant variables that further were optimized via 33 Box-Behnken Design of Experiment (DOE). Resultant nanoparticles have desired stability, entrapment efficiency, skin permeability, and sustained drug release pattern at pH 6.5 (arthritic joint pH). Moreover, cellular uptake of the prepared nanocarrier system was assessed by using Rhodamine-B loaded nanoparticles. MTT assay confirmed cellular biocompatibility with minimal toxicity. Thus, the QbD-based approach had successfully led to the fabrication of Tofa-nHA-GLT NPs with potential to target the inflamed arthritic joint.

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Auto Mode Biomimicry: A Versatile Theranostic Model for an Efficient Tumor Targeting

I. Tariq[1]
[1] Punjab University College of Pharmacy, University of The Punjab, 54000 Lahore, Pakistan.

Article Info

Keywords:
Mesenchymal Stem cells, Photodynamic therapy, Theranostics.

Abstract

Upon light irradiation, a photochemical process can produce reactive oxygen species (ROS) to cause a permanent destruction of the tumor cells. The cell-drug based biomimicry was developed using mesenchymal stem cells for a potential theranostic approach for the delivery of photosentizer to the targeted tumor cells. In vitro characterization, tumor taxis, penetration, photo induced cytotoxicity under dark and light stimulatory conditions were evaluated in non small cells lungs carcinoma models. The photosensitizer camouflaged nanocarrier laden mesenchymal stem cells (MSCs) exhibited a significant tumor migration ($P>0.001$), infiltration into the tumor cells and a substantial tumour destruction after photodynamic therpay ($P>0.01$). These findings suggest that this biomimetic technology might be valuable option not just for cancer treatment but also for the variety of other biomedical applications.

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Cotton Candy Medicine: An Innovative Tool for Designing Palatable Formulation for Pediatric Patients

A. Hussain[1], S. Nasir, F. Hussain, M. Owais and M. Muratab
[1] Punjab University College of Pharmacy, University of The Punjab, 54000 Lahore, Pakistan.

Article Info

Keywords:
Centrifugal Melt Spinning,
Dissolution Enhancement,
Microfibers,
Cotton Candy Medicine.

Abstract

Cotton candy medicine are produced via centrifugal melt spinning (CMS) that produces micro-fibers from the molten mixture containing drug in a suitable base. The aim of this project was to fabricate fibrous solid dispersion of drugs for the improved dissolution rate and hence quick therapeutic action and improved palatability. The methodology include i) screening of machine and formulation parameters ii) drug loading in microfibers iii) In-vitro characterization of fibers. iv) dosage form design and characterization (in-vivo, in-vitro). Drug incorporated in microfibers showed rapid in-vitro and in-vivo (oral) dissolution. Sucrose based formulation masked taste hence good for pediatric patients. CMS proved to be one step, simple, economical safe and effective method to fabricate fibers in micrometer range. This technology would benefit the patients and clinicians in providing customized novel dosage form. Cotton candy medicine is very recent concept that requires an insight by developing and validating different dosage forms**. Our group is the first ever in Pakistan using this technology in pharmaceutical product design.**

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Faculty of Pharmacy, Capital University of Science and Technology, Kahuta Road, Islamabad Pakistan.
Ph. # +92-51-111-555-666 **Email:** i-cetps@cust.edu.pk