Compendium of Research Publication

DEPARTMENT OF PHARMACY

2015

Sumandeep Vidyapeeth

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Message of Principal

I am pleased to present fourth annual research compendium of Department of Pharmacy which a compilation of research and development activities conducted in a calendar year. This compendium comprises of detailed information of the publication, ongoing and completed research projects, number of workshops and seminars conducted and attendant by the students and the faculties.

In continuing the dedication of the researchers and the research scholars, Department of pharmacy is aiming to set a matured research institution where our students will get excellent training so that they can compete in the field with other competitors. Pharmacy field is now becoming more research oriented which needs to facilitate the department with sophisticated instruments. This year the stress has been given to the molecular biology research and it has been decided to establish a molecular biology research laboratory. Departmental research committee has decided to proceed in this area and suggested to purchase PCR so that such good project involving molecular biology investigation can be performed and the outcomes can be published in high impact factor journals. The Department has able to get some of industrial projects in collaboration which enhances the confidence of our researchers and research scholars.

This is the fourth research annual compendium which reflects our continuous strength and hard work showing inclination of the students and the faculty towards the research in various fields of pharmacy. In order to enhance the research environment, our university has framed the research incentive scheme. The enthusiasm of our dedicated faculties has been to encourage our students to do the high impact research projects. I assure that this encouragement and commitment of the faculties of the department will be continued in the time to come. I would like to compliment all the researchers and the researcher scholars who have contributed their knowledge and the novel research ideas at the department. I also congratulate the compilation team to bring this compendium as the ready reference of our dedication towards research and development.

Dr. A K Seth
Principal / HOD,
Department of Pharmacy,
Sumandeep Vidyapeeth,
Piparia, Vadodara

Contents

Research Policy

Introduction

This policy establishes the research environment within which academic staff and postgraduate research students carry out their research. It also provides an overarching framework for the development and implementation of all research management at Sumandeep Vidyapeeth

Objectives

- To develop a proactive mechanism for smooth implementation of research projects.
- To promote research culture among the staffs and students of the university.
- Simplification of procedures like sanctions/purchases for research projects and other aspect.
- To motivate researchers to apply for external funding agency.
- To promote the publication from all research projects.

Practices

- Central research committee circulates the notification regarding inviting research projects from the students and staff of each constituent unit of university twice in a year.
- Interested candidates write a research proposal in the prescribed format provided by central research committee and submit it to central research committee in given time limit.
- Research scholar can also apply for the research fellowship/ financial assistance / grant to university / External agency as per procedure guideline given by central research committee.
- Central research committee reviews the research projects thoroughly scrutinizes the submitted projects, identifies the need of research projects & thrust areas of research project submitted by research student/faculty/scholar of the respective department.
- The research projects which fulfill the entire criterion and satisfy the research thrust possessing will be considered for funding.
- The Central research committee will call external experts for reviewing of projects.
- The principal investigator has to obtain the SVIEC permission before commencement of the research work.
- The Principal investigator should commence his/her project at the pre-decided date and complete in a stipulated time period.
- The Principal investigator must follow the SV instrument purchase procedure for any procurement of instrument/equipment.

- Minimum one fourth grant will be disbursed at the initial stage and subsequently further installments will be disbursed on submission of utilization certificate along with bills and account statement of the previous grant.
- The First installment will be disbursed with a written application for grant with SVIEC letter to Director Research Cell.
- All communication related to grant utilization or withdrawal of installments shall route through Director, Research Cell.
- Any patent generated by research work under this scheme will be shared with Sumandeep Vidyapeeth.
- In all publications, it is mandatory to include the name of Sumandeep Vidyapeeth.

Grant / Incentive received for research

Sr. no.	Name of Faculty	Category for grant/incentive received	Amount in Rs
1.	Mr Nirmal Shah	Paper publication	10,000/-
2.	Dr Rajesh Maheshwari	Paper publication	22,500/-
3.	Mrs. Arti Zanwar	Paper publication	7,500/-
4.	Dr.Ujjwal Sahoo	Paper publication	15,000/-
5.	Dr. Yogesh Yadav	Paper publication	5,000/-
6.	Mr. Sachin Chauhan	Paper publication	5,000/-

Ongoing research projects

Sponsored research projects			
Sr. no	**Name of the project**	**Name of the funding agency**	**Total grant received (Rs in Lakhs)**
1	Biochemical and Pharma-cological investigation of some antidiabetic and AntiHyper lipidemic drugs in combination with antioxidants on the levels of adipocytokines in metabolic syndrome	Research Cell, Sumandeep Vidyapeeth	40.32 /-
2	Pharmacognostic profile and pharmacological effects of different parts of *Moringa oleifera* plants		34.50 /-
3	Phytopharmacological screening and formulation development of some medicinal mushroom	GUJCOST	1.65 /-
Faculty research projects			
1	Mrs. Aarti Zanwar	Analytical method development and validation of some drugs combinations	
2	Mr. Ghanshyam Parmar	Pharmacognostic and pharmacological standardization of some Euphorbias plants.	

Completed research projects

Students research projects		
Sr no	**Name of student**	**Title of the project**
1.	Roshni Gupte	Development and prospective process validation for manufacturing process of aceclofenac tablet
2.	Anupama Sharma	Effect of coenzyme Q10 alone and its combination with Pentoxifylline in cisplatin induced nephrotoxicity
3.	Arpit Jariwala	Development and characterization of albuminal and conformal coating for implantable medical device
4.	Dhiral Patel	In vitro diffusion enhancement of Cilnidipine by nanonization
5.	Jainab Patel	Formulation and evaluation of microemulsion loaded gel of naproxen or topical delivery
6.	Chirag Patel	Formulation and evaluation of propanalol HCl loaded hydrogel beads
Faculty research projects		
1.	Dr. Rajesh Maheshwari	Effects of coenzyme Q10 with antidiabetic and antihyperlipidemic drugs in experimental induced diabetic complication.
2.	Dr. Ujjwal Sahoo	Design synthesis and pharmacological evaluation of novel oxadiazole, triazole and thiazolidinone-4-one
3.	Mr. Sachin Chauhan	Design development optimization and evaluation of nanoparticulate drug delivery system of some anticancer drug.
4.	Mr. Nirmal Shah	Techniques to improve bioavailability of Selective Estrogen Receptor modulators (SERMs) for treatment of osteoporosis
5.	Mr. Ashim Kumar Sen	Development and validation of new analytical methods of some group of pharmaceuticals from its bulk and pharmaceutical dosage form
6.	Mrs. Dhanya Sen	Development and validation of new analytical methods of some antihypertensive and antidiabetic group of pharma-ceuticals from its bulk and pharmaceutical dosage form
7.	Mr. Girish Sailor	Design development optimization and evaluation of novel drug delivery system of some phytopharmaceuticals.
8.	Mrs. Falguni B Tandel	Analytical method development and pharmacokinetic study of some new anti-inflammatory agents
9.	Mr. Ankur Javia	Design, development and characterization of colon cancer targeting folic acid conjugated Capecitabine nanoparticles
10.	Mr. Chintan Aundhia	Formulation design and development of nano carrier system for treatment of osteoporosis

Maheshwari RA, Balaraman R, Sen AK, Chandrakar VR. Effect of coenzyme Q10 alone and its combination with rosuvastatin on streptozotocin-nicotinamide induced diabetic neuropathy in rats. International Journal of Pharmacy and Pharmaceutical Sciences. 2014;7(1):296-299.

Abstract

Objectives: This study was aimed to investigate the effect of coenzyme Q10 and its combination with Rosuvastatinon STZ-nicotinamide induced diabetic neuropathy. **Methods:** Diabetic neuropathyin rats were induced with streptozotocin - nicotinamide. The diabetic rats were treated with coenzyme Q10 or rosuvastatin or their combination. Various parameters like muscular grip strength, paw withdrawal response, tail flick response and markers of oxidative stress such as malondialdehyde (MDA) level, superoxide dismutase (SOD) and reduced glutathione (GSH) in the sciatic nerve were measured. All treated animal was subjected to histopathological changes of sciatica nerve. **Results**: In diabetic control group, muscular grip strength was significantly decreased and increased paw withdrawal response, tail flick response ascompared to normal control rats. In addition, STZ-nicotinamide caused nerve cell damage with a higher MDA level, depletion of SOD and GSH level along with marked degeneration ofthe nervecell. The treatment of diabetic rats with coenzyme Q10 orrosuvastatinor their combination ameliorate STZ-nicotinamide induced nerve damage due to improvement inthe muscular grip strength, paw withdrawal response, tailflickresponse, reduction in oxidative stress along with histopathological changes. Conclusion: This finding suggests that treatment with coenzyme Q10 or rosuvastatin showed significant neuroprotective effect against STZ-nicotinamide induced diabetic neuropathy. However, concomitant administration of both showed a better neuroprotective effect thancoenzymeQ10 or rosuvastatin alone treatment.

Keywords: Diabeticneuropathy,CoenzymeQ10, Rosuvastatin, Musculargrip strength, Oxidativestress**.**

Agrawal R, Maheshwari R, Balaraman R, Seth A, Konduri P, Sankar VS. Anti-hyperglycemic and Anti-lipidemic activities of Diabac (a polyherbal formulation) in Streptozotocin-nicotinamide induced type 2 diabetic rats. Pharmacognosy Journal. 2015;7(5):283-288.

Abstract

Aim: The objective of the work was to investigate the antidiabetic activity of Diabac (a polyherbal formulation) in streptozotocin-nicotinamide induced type 2 diabetic rats. **Methods:** Oral glucose tolerance test (OGTT) was performed to evaluate effect of Diabac on elevated glucose level. The type 2 diabetes was induced by overnight fasted rats by a single intraperitoneal (i.p.) injection of 65 mg/kg streptozotocin, 15 min. after the i.p. administration of 110 mg/kg nicotinamide. The diabetic rats were treated with Diabac (250, 500 and 1000 mg/kg, p.o.) or glibenclamide (5 mg/kg, p.o) for four week. Various parameters were studied such as fasting blood sugar level, serum insulin levels, glycated hemoglobin (HbA 1C), serum lipid levels, serum creatinine, urea, uric acid and liver glycogen. **Results:** Treatment with Diabac significantly reduced the blood sugar levels in OGTT. Diabetic rats showed a significant increase in the levels of glycated hemoglobin, serum lipids, serum creatinine, urea and uric acid, whereas there was a decrease in serum insulin, liver glycogen and HDL-C levels as compared to normal control rats. The administration of Diabac or glibenclamide significantly decreased the levels of glycated hemoglobin, TG, TC, LDL-C, serum creatinine, urea and uric acid, whereas there was an increase in the levels of liver glycogen and HDL-C as compared to diabetic control rats. However, the treatment with Diabac did not show any significant change in serum insulin levels as compared to diabetic control rats. **Conclusion:** These results of present study concluded that Diabac has anti-diabetic and anti-lipidemic activities which are responsible for its use in traditional medicine.

Keywords: Diabac, Glycated hemoglobin, Liver glycogen, Serum lipids, Streptozotocin

Sahoo U, Seth A, Balaraman R, Velmurugan R. Design, Synthesis of Some Novel Thiazolidin-4-one Derivatives Bearing Benzimidazole Nucleus and Biological Evaluation of their Possible in vitro Antiinflammatory as Cyclooxygenase Inhibitors and Antioxidant Activity. Asian Journal of Chemistry. 2015;27(3):961.

Abstract

A series of 2-[2-(4-cyanophenyl)-6-substituted-1H-benzimidazol-1-yl]-N-[2-(substituted)-4-oxo-1,3- thiazolidin-3-yl]acetamide [9(I-XXXI)] were synthesized. Substituted o-phenylenediamine was reacted with substituted 4-cyanobenzaldehydes in the presence of sodium metabisulfite to furnish substituted 2-(4-cyanophenyl)-1H-benzimidazoles (1). When these substituted 2-(4-cyanophenyl)-1H-benzimidazoles were further treated with ethyl chloroacetate in KOH/DMSO, N-alkylated product (2-(4-cyanophenyl)-benzimidazol-1-yl)-acetic acid ethyl esters (2) was formed. To synthesize 2-(4-cyanophenyl)-benzimidazol-1-yl-acetic acid hydrazides (3) chemical reactions were conducted between hydrazine hydrate and the esters (2). When a mixture of 2-(4-cyanophenyl)-benzimidazol-1-yl)-acetic acid hydrazide (3) react with substituted aldehydes in ethanol was reflux, imines intermediates [4(I-XXXI)] was formed. To synthesize 9(I-XXXI) reactions were occurred between a mixture of imine intermediate and thioglycollic acid in dioxane. The structures of newly synthesized compounds 9(I-XXXI) was confirmed by spectroscopic techniques. All the synthesized compounds were screened for its in vitro antioxidant and antiinflammatory activity. The in vitro antioxidant and antiinflammatory activity might be attributed due to the presence of more electrons withdrawing group and moiety having more lipophilicity also more electronegativity in nature.

Keywords: O-Phenylenediamine, 4-Cyanobenzaldehyde, Thiazolidinone, Antioxidant, Antiinflammatory.

Sailor G, Seth A, Parmar G, Chauhan S, Javia A. Formulation and in vitro evaluation of berberine containing liposome optimized by 32 full factorial designs. Journal of Applied Pharmaceutical Science Vol. 2015;5(7):023-8.

Abstract

The present study demonstrates the application of 3^2 full factorial design for optimization of berberine loaded liposome for oral administration. Thin film hydration method was used to prepare liposome and optimization was done by 3^2 full factorial designs combined with desirability function. Nine formulations were prepared by using different drug: lipid and soyphosphatidylcholine: cholesterol (SPC:CHOL) ratios and evaluated for entrapment efficiency and vesicle size. The statistical validity of model was done by analysis of variance (ANOVA). Response surface graph and contour plots were used to understand the effect of variables on responses. The optimized formulation with 0.782 desirability value was prepared and evaluated for responses. The results of entrapment efficiency and vesicle size were found to be very close with the predicted values. In addition, an optimized formulation was also characterized for zeta potential, in vitro drug release and morphology. The formulation was found to be spherical shape with an average diameter of 0.823 nm and -1.93 mV zeta potential and also shows sustained release pattern. These results support the fact that 3^2 full factorial designs with desirability function could be effectively used in optimization of berberine loaded liposome.

Keywords: Berberine; 3^2 full factorial design; desirability function; lipid based formulation

Ashim K Sen, Dhanya B Sen, Rajesh A Maheshwari, R Balaraman, A K Seth. Quantitative simultaneous determination of aliskiren hemifumarate and hydrochlorothiazide in combined tablet formulataion by RP-HPLC. International journal of pharmacy and pharmaceutical sciences. 2015;7(8):142-145.

Abstract

Objective: Development and validation of quantitative simultaneous determination of aliskiren hemifumarate (ALI) and hydrochlorothiazide (HCT) in combined tablet formulation by RP-HPLC. **Methods:** The separation of components was achieved on Enable C 18 **Results:** Linear concentration range was between 1.2-240 µg/ml for ALI and 0.1 -20 µg/ml for HCT and correlation coefficient was found to be 0.9995 and 0.9998, respectively. The limit of detection and limit of quantification for ALI was found to be 0.3376 and 1.0230 µg/ml and for HCT 0.0288 and 0.0873 µg/ml, respectively. The results of precision (% RSD<2) studies showed good reproducibility. Recovery study was performed at 50, 100 and 150 % level to check the interferences between analytes and formulation excipients and % recovery was found to be 99.49 ±0.9868 for ALI and 99.87 ±0.8556 for HCT. The percentage assay was found to be 100.36 ±0.9201 and 99.40 ±0.7624 for ALI and HCT, respectively. column (250×4.6 mm, 5 µm) with a mobile phase consisting of 0.2 % v/v triethylamine in water(pH 6 was adjusted with orthophosphoricacid): methanol (10:90 %v/v) at a flow rate of 1 ml/min was employed. Quantification was achieved with PDA detection at 280nm. Validation parameters of the proposed method such as specificity, linearity, accuracy, precision and robustness were evaluated according to ICH guidelines. **Conclusion:** A simple, rapid, cost effective and highly sensitive RP-HPLC method as compared to existing methods for the determination of ALI and HCT in tablet formulation was developed and validated as per ICH guidelines. The method uses simple reagents and sample preparation procedures were minimal. Thus, the proposed method can be applied for routine quality control determination of ALI and HCT in tablet formulation.

Keywords: Aliskiren hemifumarate, Hydrochlorothiazide, RP-HPLC, Tablet formulation.

Sen DB, Sen AK, Zanwar A, Balaraman R, Seth A. Determination of alogliptin benzoate and metformin hydrochloride in tablet dosage form by simultaneous equation and absorption ratio method. International Journal of Pharmacy and Pharmaceutical Sciences. 2015;7(8): 380-383.

Abstract

Objective: Development and validation of two simple, rapid, accurate and sensitive UV-spectrophotometric methods for simultaneous estimation of alogliptinbenzoate (ALO) and metformin hydrochloride (MET) in bulk and tablet dosage form. **Methods:** First method (Method A) is simultaneous equation method, which is based on the measurement of absorption at 224 nm and 237 nm for both ALO and MET, respectively. Second method (Method B) is an absorption ratio method, which is based on the measurement of absorption at 251 nm i.e. Isoabsorptive point of ALO and MET and 224 nm which is λmax Results: Both the drugs were found to be linear in the concentration range of 0.5-18 µg/ml and correlation co-efficient was found to be 0.9998 and 0.9992 for ALO and 0.9998 and 1 for MET at 224 nm and 237 nm, respectively for simultaneous equation method. For absorption ratio method, both the drugs were found to be linear in the concentration range of 0.5-18 µg/ml and correlation co-efficient was found to be 0.9998 and 0.9997 for ALO and 0.9998 and 0.9997 for MET at 224 nm and 251 nm, respectively. Recovery studies at 50, 100 and 150% levels were carried out to assess accuracy of the methods . Precision studies were also carried out and %RSD was found to be within the limit (% RSD<2). The percentage assay (Method A) was found to be 100.57±1.1367 and 101.24±1.0936 for ALO and MET, respectively. For Method B, percentage assay was found to be 101.46±0.7160 for ALO and 100.15±0.6953 for MET. **Conclusion:** The developed methods were found to be simple, rapid, accurate and sensitive. Therefore, both the methods can be successfully applied for simultaneous determination of ALO and MET in tablet formulation.

Keywords: Alogliptin benzoate, Metformin hydrochloride, Simultaneous equation method, Absorption ratio method

Shah N, Seth A, Balaraman R. Bioavailability enhancement of poorly soluble raloxifene by designing inclusion complex with β–cyclodextrin. International Journal of Pharmacy and Pharmaceutical Sciences. 2015;7(8):205-211.

Abstract

Objective: Raloxifene hydrochloride (RLX) is widely used in the treatment of osteoporosis, but due to its extensive first pass metabolism bioavailability of RLX is remaining only 2%. In addition of that being from BCS class II, RLX has poor water solubility. Therefore the objective of present research work was to enhance solubility and dissolution rate of RLX by formulating inclusion complex with β cyclodextrin (β-CD) as a carrier. **Methods:** Inclusion complex was prepared by various methods like physical mixture, co-precipitation method and kneading method using different drug to carrier ratios (1:1, 1:2 and 1:3). **Results:** Inclusion complex prepared with co-precipitation method had shown 5.5 fold improvements in water solubility and significant increment in dissolution rate when compared with plain RLX. Optimized formulation was characterized by Fourier transform infrared spectroscopy, Differential scanning calorimetry, X-ray diffraction and Scanning electron microscopy studies for their compatibility, thermal analysis, crystallinity and surface morphology determination, respectively. Results of DSC and XRD study suggested the conversion of RLX from crystalline form to amorphous form. Stability studies showed stable formulation up to the period of 6 months. *In vivo* pharmacokinetic study was also conducted in wistar rats for optimized drug loaded inclusion complex that showed nearby two fold increments in drug bioavailability compared to plain drug suspension. **Conclusion:** From these studies, it can be concluded that solubility and dissolution rate of poorly soluble raloxifene could be remarkably increased by formulating into the inclusion complex with β-CD which results in significant improvement in bioavailability of poorly soluble RLX.

Keywords: Bioavailability, Dissolution rate, BCS classification, Inclusion complex, Carrier.

Shah S, Sailor G, Shah N, Chauhan S, Aundhia C, Seth A. Formulation and evaluation of irbesartan loaded solid lipid nanoparticles by solvent injection method. Pharma Science Monitor. 2015;6(1): 36-72.

Abstract

Solid lipid nanoparticles (SLNs) are a colloidal carrier system for controlled drug delivery. The purpose of this work was to prepare solid lipid nanoparticles (SLNs) of poorly water soluble drug Irbesartan (IRB). The SLNs were prepared using stearic acid as a lipid by solvent injection method by applying 3^2 full factorial designs. Two variables, polyvinyl alcohol concentration and amount of lipid were found to have significant effect on the entrapment efficiency (EE), drug loading (DL) and in vitro drug release of the SLNs. The optimized batch was also evaluated for its particle size, zeta potential and surface morphology. In addition, optimized formulation was also compared for in vitro drug release with drug solution. The results indicated the sustained release properties of prepared SLNs. Thus, the IRB loaded SLNs would be useful for delivering a poorly water soluble IRB which may beneficial in improving bioavailability and antihypertensive efficacy.

Keywords: Solid lipid nanoparticles, Irbesartan (IRB), Solvent injection method

Solanki G, Shah N, Chauhan S, Aundhia C, Javia A, Seth A. Formulation and evaluation of cyclophosphamide loaded chitosan nanoparticles conjugated with folic acid for cancer targeting. Pharma Science Monitor. 2015;6(1): 171-189.

Abstract

Over the past decade, there has been increasing interest in using nanotechnology for cancer therapy. The development of smart targeted nanoparticles that can deliver drug at a sustained rate directly targeted to cancer cell may provide better efficacy and lower toxicity for treating primary and advance metastatic tumor. Recently, Chitosan nanoparticles have been intensively investigated as a novel drug carrier due to their extensive advantages, such as good biocompatibility, biodegradability and non-toxic properties. The rational of this study was to prepare cyclophosphamide loaded folate-chitosan conjugated nanoparticles (FA-CS NPs) for improving tumor- targeted drug delivery. The Chitosan nanoparticles were prepared by ionic cross linking method which improve the efficiency of anticancer drug delivery and folic acid (FA) was conjugated with CS NPs by electrostatic interaction between cationic amino group of Chitosan and anionic carboxyl group of FA. The processing parameters involved in the method were optimized, including different concentration of polymer (Chitosan) and cross linking agent (TPP). The NPs were evaluated for entrapment efficiency, particle size, drug release for 24 hrs and stability study for 3 months. Results of optimized batch B8 was found for %EE 89.74±2.36 and drug release 92.4±2.15. During stability study, the NPs found to be stable. So, it can be conclude that the FA-CS NPs can be used for potential targeting delivery of anticancer drugs.

Keywords: Nanoparticles, cyclophosphamide, ionic cross linking, bioavailability.

Yadav YC. Hepatoprotective effect of Ficus religiosa latex on cisplatin induced liver injury in Wistar rats. Revista Brasileira de Farmacognosia. 2015;25(3):278-283.

Abstract

Ficus religiosa L., Moraceae, is widely planted in the tropics. The chemical constituents of *F. religiosa* include tannin, saponin gluanol acetate, β-sitosterol, leucoanthocyanidin, and leucoanthocyanin. These are used for the treatment of pain, inflammation, impotence, menstrual disturbances, and urine related problems, and as uterine tonic. The present study aimed to evaluate hepatoprotective effects of *F. religiosa* latex on cisplatin induced liver injury in Wistar rats. In experimental protocol contained five groups of rats (n = 6). In which, group I (control) was administered acacia (2%, w/v) of 5 ml/kg throughout the experiment for 16 days. The group II (cisplatin treated) was administered single dose of cisplatin (7.5 mg/kg *i.p.*) on 1st day. Group III (extract control) was administered 300 mg/kg *p.o.* of extract for 1st to 10th day. Group IV (Protective) was administered extract (300 mg/kg *p.o.*) of *F. religiosa* latex for 1st to 10th day and administered single dose of cisplatin (7.5 mg/kg *i.p.*) on 11th day and group V (Curative) received single dose of cisplatin (7.5 mg/kg *i.p.*) on day 1st, and administered extract (300 mg/kg *p.o.*) from 7th to 16th days. On the 6th day in cisplatin treated, 10th day in extract control and 16th day in control, protective and curative, blood withdrawn from retro-orbital sinus of rats for biochemical estimation for serum and dissected out the livers for estimation of antioxidant enzymes and histopathological works. The cisplatin-treated group 2 showed a significant increase in serum alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and hepatocytes cells degeneration inflammatory infiltrate and necrosis it's were significantly (**$p < 0.01$) alleviates by protective groups.

Keywords: Hepatoprotective, *Ficus religiosa* latex, Cisplatin, Liver injury

Rajesh A Maheshwari, R Balaraman, Girish U Sailor, Dhanya B Sen. Protective effect of simvastatin and rosuvastatin on trinitrobenzene sulfonic acid-induced colitis in rats. Indian Journal of Pharmacology. 2015;47(1): 17-21.

Abstract

Objective: Statins have anti-inflammatory effects that are not directly related to their cholesterol lowering activity. This study was carried out to evaluate the effect of simvastatin or rosuvastatin on the extent of colonic mucosal damage and on the inflammatory response in trinitrobenzene sulfonic acid (TNBS)-induced ulcerative colitis. **Materials and Methods:** Ulcerative colitis was induced by single intrarectal injection of 120 mg/kg TNBS. Test groups were treated with simvastatin (10 mg/kg, p.o.) or rosuvastatin (10 mg/kg, p.o.). Colonic mucosal inflammation was evaluated clinically, biochemically, and histologically. **Result:** Disease activity index score in TNBS-treated rats, as determined by weight loss, stool consistency, fecal occult blood, were significantly lowers in simvastatin or rosuvastatin-treated rats than TNBS-treated animals. Simvastatin or rosuvastatin counteracted the reduction in colon length, decreased colon weight, neutrophil accumulation, and tumor necrosis factor-alpha level in TNBS-induced colitis. Simvastatin and rosuvastatin also inhibited the increase in oxidative stress levels after TNBS administration. **Conclusions:** These results suggest that simvastatin and rosuvastatin significantly ameliorate experimental colitis in rats, and these effects could be explained by their anti-inflammatory and antioxidant activity.

Keywords: Rosuvastatin, simvastatin, trinitrobenzene sulfonic acid, tumor necrosis factor-α, ulcerative colitis

Maheshwari R, Pandya B, Balaraman R, Seth AK, Yadav YC, Sankar VS. Hepatoprotective effect of Livplus-A polyherbal formulation. Pharmacognosy Journal. 2015;7(5): 311-316.

Abstract

Objective: The aim of the present study was to investigate the hepatoprotective effect of Livplus (a polyherbal formulation) against CCl4-induced hepatotoxicity in rats. **Methods:** Hepatotoxicity was induced in rats by i.p. injection of CCl4 once three days for 14 days. Livplus or Silymarin was administered along with CCl4 and the biochemical parameters like as partate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin (TB), direct bilirubin, total protein (TP), gamma-glutamyl transferase (GGT), total cholesterol (TC) and triglycerides (TG) were estimated. Furthermore, biomarkers of oxidative stress such as MDA levels, Glutathione contents, SOD and catalase activity in liver tissue were estimated. **Results:** Treatment with Livplus significantly reduced the elevated levels of ALT, AST, ALP, bilirubin (direct and total), GGT, TC, TG and increased levels of TP compared to CCl4 control rats. The treatment with Livplus also showed a significant increase in glutathione contents, SOD and catalase activity and a decrease in MDA levels compared to CCl 4 control rats. **Conclusion:** The finding of present study indicates that Livplus showed a potential hepatoprotective activity. These results support the traditional use of Livplus in the treatment of liver disorders.

Keywords: Livplus, CCl4 Hepatotoxicity, GGT, Hepatic enzymes.

Gadhvi Ishwardan, Patel parteek, Gurav Nilesh, Sen Dhanya. RP-HPLC Method development and validation for estimation of Withaferin A in polyherbal formulation. Inventi rapid:Pharma Analysis & Quality assurance. 2015;1: 24-28.

Abstract

A simple, rapid and specific reversed-phase HPLC method has been developed for analysis of withaferin-A in a polyherbal formulation containing Withania somnifera extracts. HPLC analysis was performed on a C18 column using a 60:40 (v/v) mixture of acetonitrile and water as isocratic mobile phase at a flow rate of 1 ml/min. UV detection was at 230 nm. The method was validated for accuracy, precision, linearity, specificity and sensitivity in accordance with international conference on harmonization guidelines. Validation revealed that method was specific, accurate, precise, reliable and reproducible. Good linear correlation coefficients (r2>0.9993) were obtained for calibration plots in the ranges. Limit of detection was 0.05 and limit of quantification was 0.16 ?g. Intra and inter-day RSD of retention times and peak areas were less than 2%. Recovery was between 98.15 and 100.69% obtained for withaferin-A. The established HPLC method was appropriate and withaferin-A was well resolved. The method was successfully used for quantitative analysis of withaferin-A in a polyherbal formulation.

Sachin Chauhan, AK Seth, NV Shah, CJ Aundhia, AR Javia, GU Sailor. Formulation and In Vitro Characterization of Anastrozole Loaded Nanoparticles with Factorial design Based Studies. American journal of pharmatech research. 2015;5(3): 539-554.

Abstract

The purpose of this study was to develop chitosan based anastrozole nanoparticles for treatment of breast cancer. An ionic gelation method was used to prepare anastrozole controlled-release nanoparticles. A 3^2 full factorial design was employed. Experimental variables such as concentration of CS and cross-linking agent sodium TPP were varied to study their effect on drug entrapment efficiency and release rates of drug from nanoparticles. Fourier transform infrared spectroscopic (FTIR) analysis and differential scanning calorimetry (DSC) were employed to determine any interactions between drug and polymer. The FTIR studies revealed no chemical interaction between the drug and the polymer. Entrapment efficiency of nanoparticles ranged between 51.51 ± 0.81 % to 84.35 ± 1.06 %.In-vitro release studies were performed in phosphate buffer saline of pH 7.4. A slow release of anastrozole up to 72 h was observed. Mean particle size of nanoparticles ranged between 1635 nm to 72.30 nm with mean particle size of 273.6 nm, while zeta potential 0.52 mV. DSC results indicated that the anastrozole entrapped in the nanoparticles existed in an amorphous or disordered-crystalline status in the polymer matrix. Scanning electron microscopy was done to study the surface morphology. Results revealed that more spherical shaped particles with possible aggregation. The highest correlation coefficients were obtained for the Higuchi model, suggesting a diffusion mechanism for the drug release. The results demonstrated that anastrozole nanoparticles with chitosan could be an alternative delivery method for the long-term treatment of breast cancer.

Keywords: Anastrozole; Nanoparticles; Factorial design; Ionic gelation; Controlled release

Ankur Javia, A.K.Seth. Development and Optimization of Capecitabine Loaded Chitosan Nanoparticles for Colon Cancer Therapy. American journal of Pharmtech Research. 2015;5(4): 709-723.

Abstract

The goal of this study was to develop and optimize the Capecitabine loaded chitosan nanoparticles (CS-NPs)for improved colon cancer therapy, by enhancedsurface area, sustained drug release, reduced dose and hence, most importantly, reduced toxicity. Capecitabine loaded Chitosan nanoparticles were prepared by 3^2 full factorial designs, using ionotropic gelation method by cross-linking of chitosan (CS) with sodium tripolyphosphate (TPP). CS-NPs were prepared by dissolving chitosan in 1% (w/v) acetic acid solution under magnetic stirring at room temperature. The CS solution was diluted with deionized water to produce different concentration. The capecitabine was dissolved in CS solution using sonication and aqueous TPP solution was added drop wise using syringe to the mixture with moderate stirring for 30 min. The prepared nanoparticles were characterized by FT-IR spectroscopy and DSC to confirm the cross linking reaction between CS and cross-linking agent. From the % entrapment of capecitabine, nanoparticles were optimized using regression analysis, contour plots and check point analysis. Particle size of the optimized batch (CS-NPs-8) was found to be 87 nm. The Polydispersity index of the nanoparticles was found to be 0.113. The nanoparticles formed were spherical in shape with high zeta potentials, -35mV. *In vitro* release studies in phosphate buffer saline (pH 7.4) showed an initial burst effect and followed by a slow drug release. The drug release followed first order kinetics and was found to be diffusion controlled. Optimized formulation was also showing more % inhibition than drug alone in *In-vitro* anticancer study. From the accelerated study of optimized batch, it was found to be stable.

Keywords: Capecitabine, Colon cancer, Chitosan-TPP nanoparticles, HT-29

Chintan Aundhia, Avinash Seth, Sachin Chauhan, Nirmal Shah, Ankur Javia. Bioavailability enhancement of Risedronate Sodium by formulation of Nanoparticles for treatment of osteoporosis. American Journal of Pharmaceutical Research. 2015;5(4): 738 – 750.

Abstract

The present research work focuses on improving the bioavailability of the anti osteoporotic drug Risedronate Sodium. This drug belongs to BCS class III which implies that it is permeability rate limited. Hence an attempt was made to reduce the particle size to nano dimensions using ionotropic gelation technique. In this technique, chitosan was used as the polymer and sodium Tri poly Phosphate was used as the cross linking agent. The resulting nanoparticles were optimized using 3^2 full factorial design and characterized for their entrapment efficiency, percent yield, in vitro diffusion studies. The particle size and zeta potential was found out and surface morphology was studied using Scanning electron microscopy. The in vivo studies clearly showed a marked improvement in the bioavailability of the nanoparticles as compared to the plain drug suspension.

Keywords: Risedronate Sodium, Nanoparticles, Bioavailability.

Rajesh A Maheshwari, Falak Dhakwala, R Balaraman, Avinash K Seth, Hardik Soni, Ghanshyam Patel. Maxcal-C (a polyherbal formulation) prevents ovariectomy-induced osteoporosis in rats. Indian Journal of Pharmacology. 2015;47(5): 555-559.

Abstract

Objectives: The aim of the present study was to investigate the anti-osteoporotic activity of Maxcal-C in ovariectomy (OVX)-induced osteoporosis in rats. **Materials and Methods:** Sham-operated control rats were designated as Group I; Group II animals served as OVX control; Group III OVX control rats treated with Calcium Sandoz (50 mg/kg, p.o.); Group IV and V OVX control rats treated with Maxcal-C (250 and 500 mg/kg, p.o.), respectively. All the aforementioned treatments were given for four weeks after the development of osteoporosis. At the end of the treatment, serum biochemical parameters such as serum calcium and alkaline phosphate were measured. After sacrificing the animals, femoral bone parameters with histology, body weight, and bone breaking strength of 5th lumbar vertebra were measured. **Results:** The treatment with Maxcal-C showed a significant improvement in serum biochemical, femoral bone parameters, and bone breaking strength of 5th lumbar vertebra with histopathological changes. **Conclusion:** The finding of the present study indicates that Maxcal-C showed a potential anti-osteoporotic activity. These results support the traditional use of Maxcal-C in the treatment of osteoporosis.

Keywords: Bone breaking strength, femoral bone parameters, Maxcal-C, ovariectomy rats, serum calcium

Maheshwari R A, Sailor G U, Sen A K, Balaraman R. Amelioration of cisplatin-induced hepatotoxicity by statins in rats. The Journal of Integrated Health Sciences. 2015;3(1).

Abstract

Aim: This study was aimed to investigate the effect of simvastatin (SIM) and rosuvastatin (ROS) on the extent of tissue damage in cisplatin (CIS) induced hepatotoxicity. **Materials and Methods:** Hepatotoxicity was induced in rats with single intraperitoneal injection of 7 mg/kg cisplatin. Group 1 received 0.5% sodium carboxy methyl cellulose, group 2 and 3 received SIM and ROS, respectively, and group 4 was injected single dose of CIS (7 mg/kg, i.p.). Group 5 and 6 were treated with SIM (10 mg/kg, p.o.) and ROS (10 mg/kg, p.o.) daily from 5 days before to 5 day after intraperitoneal administration of CIS, respectively. Liver function tests like AST, ALT and Total bilirubin, and markers of oxidative stress such as liver malondialdehyde (MDA) level, superoxide dismutase (SOD), catalase (CAT) activities and reduced glutathione (GSH) were measured. All tissues were investigated for histopathological changes. **Results**: CIS treated rats showed a significant increase in AST, ALT and total bilirubin. Moreover, cisplatin caused liver damage with a higher MDA level, depletion of SOD, CAT activity and GSH. SIM and ROS ameliorate CIS induced liver damage due to improvement in liver function, oxidative stress, and histological alteration. **Conclusions:** These finding suggests that simvastatin and rosuvastatin may have a protective effect against cisplatin induced liver damage via amelioration of lipid peroxidation as well as due to improvement of liver function.

Keywords: Cisplatin, Simvastatin, Rosuvastatin, Hepatotoxicity

Anamika Joshi, Sachin Chauhan, A.K.Seth, Nirmal Shah, Chintan Aunndhia, Ankur Javia. Influence of formulation variable in development of floating microspheres of water soluble drug. Pharma Science Monitor. 2015;6(3):29-40.

Abstract

Floating drug delivery system for propranolol hydrochloride (PPL) was developed to prolong gastric residence time and increase drug bioavailability. The aim of present work was to prepare floating microspheres of propranolol HCl using solvent evaporation technique. Propranolol HCl is a non-selective beta adrenergic blocking agent with short elimination half life 3-5 hours. The short half life of propranolol HCl and multiple administration dose make propranolol HCl a very good candidate for formulation of floating drug delivery system. Total 27 batches were prepared by using 33 full factorial design, in which effect of drug polymer ratio, RPM and proportion of dispersion medium were studied. The prepared floating microspheres were evaluated for, particle size, percentage yield, in vitro buoyancy, drug content, entrapment efficiency, in vitro drug release, scanning electron microscopy and statistically analysed. Check point analysis was done to confirm the optimized batch. Stability of microspheres was studied as per ICH guidelines. It was observed that prepared microspheres were white, free flowing and spherical in shape. Formulation B25 prepared with drug:polymer ratio (1:5), RPM 1500 and proportion of dispersion medium(9:1) which exhibited higher percentage yield, in vitro buoyancy, entrapment efficiency and percentage drug release (96.09±0.17 %) after a period of 24 hrs. Results show that, an increase in drug polymer ratio, RPM and ratio of light liquid paraffin to n-Hexane affects the particle size, percentage yield, in vitro buoyancy and drug release of microspheres. It was observed that increase in drug polymer ratio increases the entrapment efficiency and mean particle size of the microspheres. Whereas, with the increase in RPM particle size of microsphere reduced and fine spherical shaped microspheres were produced. The data obtained in this study suggest that, floating microspheres of propranolol HCl with selected formulation variables are promising for sustained drug delivery which can reduce dosing frequency.

Keywords: Floating microspheres, Propranolol HCl, 33 Factorial design, optimization.

Sisal Shah, Dinesh G. Desai, A. K. Seth, Ronak Patel. Process validation of paracetamol suspension. Pharma Science Monitor. 2015;6(2):299-308.

Abstract

The present study was to validate the paracetamol suspension with the combination of tragacanth (0.2%) and Na.CMC (0.1%) for different mixing speed and time, the fast speed with 15 minutes showed the most satisfactory results. Hence, it can be recommended that, the same parameters shall be considered as final for further commercial routine production batches of paracetamol suspension.

Keywords: Process Validation, Paracetamol suspension, Prospective study

Charvi Patel, Dinesh G. Desai, A.K. Seth. Process validation of artemether and lumefantrine 80/480 mg tablet. Pharma Science Monitor. 2015;6(1):233-243.

Abstract

The objective of the study is to form a basis for written procedures for production and process control which are designed to assure that tablet have the identity, strength, quality and purity. It is done by checking and controlling the critical in process parameters and by evaluation of finished product. Three consecutive batches of Artemether & Lumefantrine Tablet 80/480 mg tablets were manufactured as per the Batch Manufacturing Record. Samples were collected at different stages like for sifting, blending, compression, coating, and for packaging operation as mentioned in the sampling plan for individual process. The results suggest that the all parameters are within the limits. The manufacturing process parameters like appearance, bulk and tapped density, blend uniformity and assay by using HPLC, all physical parameters like weight variation, hardness and thickness, disintegration time, friability, packaging parameters are found within the limits which indicates the process validation of Artemether & Lumefantrine Tablet 80/480 mg tablet was successfully completed.

Keywords: Artemether, Lumefantrine, concurrent process validation, wet granulation.

Dipen K. Sureja, Ghanshyam R. Parmar. Development and validation of HPTLC method for simultaneous estimation of telmisartan and indapamide in pharmaceutical solid dosage form. Journal of Chemical and Pharmaceutical Research. 2015;7(11):236-240.

Abstract

A simple, precise, accurate and specific high performance thin layer chromatographic method has been developed and validated for the simultaneous estimation of Telmisartan and Indapamide in pharmaceutical solid dosage form without separation of components. The method is based on high performance thin layer chromatographic separation of both drugs followed by the densitometric measurements at 249 nm. The separation was carried out on precoated silica gel 60 GF 254 using mobile phase hexane: ethyl acetate: methanol : glacial acetic acid (14:6:2:1 v/v/v/v) with Rf values 0.21 and 0.36 for Telmisartan and Indapamide respectively. The calibration curve was found to be linear between 2000-7000 ng/spot for Telmisartan and 75-26 2.5 ng/spot for Indapamide with correlation co-efficient 0.9970 and 0.9959 respectively. It was observed that the proposed HPTLC method could be used for efficient analysis and monitoring of the Telmisartan and Indapamide in combined pharmaceutical solid dosage forms.

Keywords: Telmisartan, Indapamide, Simultaneous estimation, HPTLC.

Nirmal shah, Ronal Patel, A K Seth, Sachin Chauhan, Sisal Shah. Solubility enhancement techiniques as a strategy to improve the solubility of Lornoxicam. Pharma Science Monitor. 2015;6(4):168-175.

Abstract

Lornoxicam is a BCS class- II non-steroidal anti-inflammatory drug (NSAID) of oxicam class that exhibits analgesic, anti-pyretic and anti-inflammatory activities. The aim of study was to enhance the solubility of lornoxicam using different solubility enhancement techniques. Three approaches viz; hydrotropy, cosolvency and mixed solvency techniques were carried out to enhance the solubility of lornoxicam. Many hydrotropes like sodium acetate, sodium salicylate, sodium ascorbate, sodium citrate, sodium benzoate, urea and nicotinamide in different molar concentration and cosolvents like polyethylene glycol (PEG), propylene glycol and glycerin in different percentage were used to enhance the solubility of poorly soluble drug. In addition to that, a mixed solvency technique was also adopted to study maximum solubility of drug. A 7.25 fold and 26 fold increase in solubility of drug was observed compared to water by using 2M nicotinamide and 40% PEG 600, respectively. Similarly, A 358 fold solubility enhancement was obtained with mixed solvency technique using mixture of 10% sodium citrate, 10% sodium benzoate, 10% nicotinamide, 5% PEG 600, 5% PEG 400 and 5% propylene glycol. The study

concluded that suitable solvent system can be developed using hydrotropy, cosolvency or mixed solvency techniques for BCS class- II category drug like lornoxicam to design suitable liquid dosage form.

Keywords: Lornoxicam, poorly soluble, mixed solvency, hydrotrope, cosolvents.

Vyas Himanshu D, Parmar Ghanshyam, Shah Nirmal, Chauhan Sachin, A. K. Seth. Formulation and evaluation of fast dissolving film of Methylcobalamin. Pharma Science Monitor. 2015;6(4):50-68.

Abstract

Over the past decade, there has been increasing interest in using sublingual route of administration. Which directly inject the dug in to the blood stream. So for drugs having less bioavailability it can be helpful to increase absorption. Also it quits the first past metabolism. Therefore drug like methylcobalamine which is having very less bioavailability when given by this route will lead to increase the absorption and at last the bioavailability. Hear by using polymers like PVA and PVP in a combination with penetration enhancer like SLS and PEG 400 as plasticizer we had prepared fast dissolving sublingual film. The result itself shows increase in the absorption (penetration) of methylcobalamine much more than given by the GI tract. Our work demonstrates that the obtained fast dissolving sublingual film of methylcobalamin can be used for the patient.

Keywords: Sublingual film, Methylcobalamine, Plasticizer, Bioavailability.

Ruchi mistry, Dinesh G. Desai, A. K. Seth. Prospective validation of tablet manufacturing process of Orodispersible tablets by direct compression. Pharma Science Monitor. 2015;6(4):69-87.

Abstract

Validation of product should be performed as per the protocol. The protocol describes the process stages, control variables & measuring responses with justification, sampling plan, acceptance criteria, summary& conclusion. During the validation, samples were withdrawn according to sampling plan. The manufacturing of orodispersible carbamazepine tablet 100 mg by direct compression was validated successfully considering the following parameters. Mixing performed in a planetary mixture for 5, 10 and 15 min at slow speed. Mix blend were sifted through 40 mesh sieve using vibratory sifter. Compression was performed on a 12 station compression machine at 13, 18, 22, 28 RPM. All the analytical data derived during process validation of carbamazepine 100 mg tablet. Hence the process is validated.

Keywords: Carbamazepine, process validation, orodispersible, direct compression.