Mucoadhesive oral drug delivery system using Natural polymer

Deepti Chauhan
Student,
Lloyd Institute of Management and Technology.

Abstract
Mucoadhesive drug delivery structures have interaction with the mucus layer masking the mucosal epithelial floor, and mucin molecules and boom the residence time of the dosage shape on the website of absorption. Mucoadhesion is generally defined as the adhesion between two materials, at the least considered one of that's a mucosal floor. Drug movements can be advanced through growing new drug delivery systems, along with the mucoadhesive machine. Those structures stay in close contact with the absorption tissue, the mucous membrane, liberating the drug at the movement web site main to a bioavailability increase and both local and systemic outcomes. Mucoadhesion is presently defined through six theories: digital, adsorption, testability, diffusion, fracture and mechanical. The mucoadhesive capability of a dosage shape is dependent upon a spread of things, including the nature of the mucosal tissue and the physicochemical properties of the polymeric components. Thus, mucoadhesive dosage paperwork are high quality in growing the drug plasma concentrations and additionally healing interest. In this regard, this evaluation covers the regions of mechanisms and theories of mucoadhesion, elements influencing the mucoadhesive devices and also numerous mucoadhesive dosage forms.

Keywords: mucus, mucoadhesion, mucoadhesiveness, dosage form, drug delivery system, oral drug delivery system.

INTRODUCTION
Oral drug delivery is the maximum applicable and favored technique of administering therapeutics agent for his or her systemic impact. similarly the oral medication is usually taken into consideration because the first avenue investigated within the discovery and development of new drug entities and pharmaceutical formulation, specially due to (Margret et al; 2009, Lachman et al; 1987)-
- affected person acceptance,
- correct dosage,
- Self – medication,
- ache avoidance,
- comfort in management and
- value effective production technique.

The treatment of infection has been achieved with the aid of administrating drug to the human body through various conventional pharmaceutical dosage forms like tablet, pill, capsules, lotions, ointments, liquids, aerosols, injectables and suppositories. Among these all the strong
oral dosage forms are more popular. In stable oral dosage forms the tablets and tablets are greater commonly employed. Tablets have benefits over tablets that they're tamper evidence dosage form. The principal hazards of capsules over tablets are their better cost. The drugs either hard pill or tender pill are prone to breakage if they may be now not stored properly. “Tablet is a unit solid dosage form containing medicinally active materials without or with appropriate diluents”. During the last hundred years tablet producers have evolved substances and tactics which could produce compressed pills containing a unique quantity of an energetic pharmaceutical ingredient (API) at high pace and at particularly low cost. experts inside the artwork of tableting are conscious with the basic art of tableting with the aid of the strategies, i.e. wet granulation, Dry granulation and Direct compression. Granulation is the system of gathering debris together by way of developing bonds b/w them. The granulation process combines one or extra powders and forms a granule with a view to permit the tableting manner to be predictable and could produce high-quality pills in the required tablet-press speed range.

The reason of present examine was to evaluate Coccinia grandis L and Chitosan for mucoadhesive properties and to formulate intestinal mucoadhesive tablet of Valsartan (model drug) to stay the dosage form within the small intestinal location for about 24 hours for the remedy of hypertension and heart failure. Prolonging the retention improves bioavailability and reduces drug wastage.

Mucoadhesive polymers are artificial or natural macromolecules which are capable of attaching to mucosal surfaces. Use of excipients from plant foundation has received importance in formula of dosage shape due to their easy availability, eco pleasant nature and fee effectiveness compared to artificial components. Mucilage extracted from fruits of Coccinia grandisL may be utilized in pharmaceutical method because of its edibility, biodegradability and biocompatibility.

Overview of Mucoadhesive Drug Delivery System

Mucoadhesion includes numerous forms of bonding mechanisms, and it is the interplay among every system that permits for the adhesive process. The predominant classes are wetting principle, adsorption concept, diffusion concept, electronic concept, and fracture concept. Specific strategies include mechanical interlocking, electrostatic, diffusion interpenetration, adsorption and fracture techniques.

Therapeutic uses:

Valsartan is an angiotensin II receptor blocker (ARB) indicated for:

- Treatment of high blood pressure, to lower blood pressure. Decreasing blood pressure reduces the hazard of deadly and nonfatal cardiovascular activities, often strokes and myocardial infarctions
- Treatment of coronary heart failure(NYHA class II-IV); diovan extensively decreased hospitalization for coronary heart failure.
• Reduction of cardiovascular mortality in clinically stable patients with left ventricular failure or left ventricular disorder following myocardial infarction.

Contraindications:
Valsartan must be used with care in glaucoma, pyloric stenosis, acute asthmatic assault and prostatism during being pregnant and lactation. Cyproheptadine hydrochloride has to now not be given to kids much less than 18 months of age.

Adverse reactions:
• Hypertension: maximum not unusual detrimental reactions are headache, dizziness, viral contamination, fatigue and stomach ache
• Coronary heart failure: maximum commonplace detrimental reactions are dizziness, hypotension, diarrhea, arthralgia, again pain, fatigue and hyperkalemia
• Post-myocardial infarction: most not unusual unfavorable reactions which precipitated patients to stop therapy are hypotension, cough and accelerated blood creatinine.
• Other side effects: consists of dizziness; headache; dose-related orthostatic hypotension; rash; angioedema; hyperkalaemia; myalgia; respiratory tract disorders; again ache; GI disturbances; fatigue; boom in BUN and serum creatinine; stomach ache; dry cough; LFT elevations.

Drug interactions:
• potassium sparing diuretics, potassium supplements or salt substitutes can also cause will increase in serum potassium, and in heart failure sufferers, will increase in serum creatinine.
• NSAID use may cause elevated chance of renal impairment and loss of antihypertensive impact.
• Dual inhibition of the renin-angiotensin gadget: increased threat of renal impairment, hypotension, and hyperkalemia.

The motive of present examine changed into to assess Coccinia grandis L and Chitosan for mucoadhesive properties and to formulate intestinal mucoadhesive pill of Valsartan (model drug) to stay the dosage form within the small intestinal location for approximately 24 hours for the treatment of hypertension and heart failure. Prolonging the retention improves bioavailability and decreases drug wastage.

Valsartan inhibits angiotensin II receptors, thereby relaxing blood vessels and causing them to widen, which lowers blood pressure and improves blood flow (3-8). it is used orally for the treatment of hypertension and has a low bioavailability of 23%, due to its poor absorption in lower gastro intestinal tract. It undergoes little or no hepatic metabolism and its removal half of life is 6 hrs. therefore, it become selected as a suitable drug candidate for the design of intestinal
mucoadhesive drugs if you want to improve its oral bioavailability and to gain subsequent reduction in its dosage and dosing frequency.

Mucoadhesive polymers are artificial or natural macromolecules that are capable of attaching to mucosal surfaces. Use of excipients from plant foundation has received significance in formula of dosage shape due to their easy availibility, eco friendly nature and fee effectiveness compared to artificial components. Mucilage extracted from end result of Coccinia grandisL can be used in pharmaceutical method due to its edibility, biodegradibility and biocompatibility.

Within the present research, an attempt becomes made to formulate intestinal mucoadhesive tablets of Valsartan using isolated novel polymer and Chitosan as polymers in numerous concentrations. To avoid mucoadhesion of the formulation within the stomach area the components need to be enteric coated. As the small intestine has relatively lesser transit time the tablet will no longer stay there for long term. Consequently, there's want to formulate once each day sustained release enteric coated mucoadhesive tablet of Valsartan which remain adhered in the small intestine for longer duration.

In the present study, intestinal mucoadhesive tablets of Valsartan were prepared by using novel natural polymer isolated from Coccinia grandis and Chitosan. For the study purpose, both of above were selected as the model polymers. The purpose of present study was to evaluate Coccinia grandis and Chitosan for mucoadhesive properties and to formulate intestinal mucoadhesive tablet of Valsartan (model drug) to remain the dosage form in the small intestinal region for about 24 hours for the treatment of hypertension and heart failure.

Valsartan is a new potent, highly selective and orally active antihypertensive drug belonging to the family of angiotensin II type 1 receptor antagonists. Valsartan inhibits angiotensin II receptors, thereby relaxing blood vessels and causing them to widen, which lowers blood pressure and improves blood flow (3-8). It is used orally for the treatment of hypertension and has a low bioavailability of 23%, because of its poor absorption in lower gastro intestinal tract. It undergoes little or no hepatic metabolism and its elimination half life is 6 hrs. Therefore, it was selected as a suitable drug candidate for the design of intestinal mucoadhesive tablets with a view to improve its oral bioavailability and to achieve subsequent reduction in its dosage and dosing frequency.

In preliminary studies, the results of IR spectra of drug and polymers showed no interference in the peaks, which indicated that, the drug and excipients were compatible with each other. The novel natural polymer was isolated from the fruits of Coccinia grandis and its characterization was performed. The results of physicochemical properties of Coccinia grandisL are shown that the Loss on Drying, Ash value and all other parameters were good. The values of angle of angle of repose, Carr’s index, Hausner’s ratio indicated that the polymer having good flow property and compressibility.

In preliminary trials initially novel polymer was used in concentrations 2.5%, 5% and 7.5%. Tablets were prepared by direct compression technique. In vitro drug release study of A1 to A3
batches showed good mucoadhesion properties. But sustained release property was not there to the required extent. Then another polymer from natural origin i.e. Chitosan was used in 2.5% concentration along with isolated novel polymer (2.5% -7.5%) was used. Tablets were prepared by wet granulation technique. PVP k-30 (4% w/v) was used as a binder. Dicalcium phosphate was used as diluent and Magnesium Stearate was used as lubricant. The tablets were prepared using 8 mm biconvex punch (Minipress 2D 8 stations). Each tablet was weighing 200 mg. In vitro drug release study showed good sustained release properties i.e. drug release upto 24h as well as improved ex vivo mucoadhesive strength.

Before compressing into tablets, granules were studied for precompression parameters, the bulk density, compressibility index which showed the excellent type of flow, Hausner’s ratio interpreted a good flow. After compression of the granules in tablets, the tablets were studied for post compression parameters such as weight variation, friability, hardness observed were well within the acceptable limits. Drug content was almost similar to all optimized batches. Drug content was found to be satisfactory.

Prepared core tablets were press coated with cellulose acetate phthalate (CAP) in different ratios (core tablet weight : weight of CAP) i.e. 1:1, 1:1.5, 1:2, 1:2.5, and 1:3 using 11 mm biconvex punch. The optimized coating ratio was found to be 1:2. The resultant weight of each tablet was 600 mg. The prepared tablets were evaluated for hardness, friability, weight variation, thickness, in vitro dissolution study, Ex-vivo residence time, Ex-vivo mucoadhesive force and drug content.

A 32 randomized full factorial design was used. In this design, 2 factors were selected each at 3 levels and experimental batches were prepared using all possible 9 combinations. In the present investigation, after carrying out preliminary trials the amount of novel polymer (X1) and amount of chitosan (X2) were selected as independent variables. All the other formulation aspects and processing variables were kept invariant throughout the study period. The Ex-vivo residence time of tablet and cumulative percentage drug release at 24 hours (Q24), were selected as dependent variables.

After analyzing both independent variables (i.e. factor) and dependant variables (i.e. response) Design Expert® software has provided number of solutions. One batch from the solutions provided by software was selected as an optimized batch based on Desirability Value i.e. Closer to one. The composition of the optimized batch is depicted in Table 6. The developed optimized batch containing 7.5 %w/v novel natural polymer and 2.5% w/v Chitosan was evaluated for various physicochemical properties. The batch F1 was selected as an optimized batch as it has shown 97.64% drug release and ex vivo residence time for about 24 h.

CONCLUSION
It may be concluded that the novel natural polymer together with chitosan shows appropriate Ex-vivo residence time, Ex-vivo bioadhesion force and sustained release properties. Therefore the polymer isolated can be used as a mucoadhesive agent. The existing study provides a new alternative that is less expensive and biocompatible formulation of Valsartan within the treatment of coronary heart failure. Therefore the present once a day method of Valsartan may also enhance the patient compliance with cost reduction.
REFERENCES


