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Research Article

Design and Characterization of Ranitidine Hydrochloride Mucoadhesive Nanoparticles for the Treatment of Peptic Ulcer

Jagadeesh Kumar Ega [1] and Kavitha Siddoju [2]*

Corresponding Author:
jkjagadeeshkumare@gmail.com

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ABSTRACT

Ranitidine Hydrochloride is pale yellow, Granular substance Soluble in water, Histamine 2-receptor antagonist and antiulcer drug. In this paper we have evaluated the drug Ranitidine Hydrochloride by Release kinetics , *In vitro* release studies ,Morphology , Poly dispensability index (PDI) , Drug entrapment efficiency And Zeta potential . The present's investigations mainly focus on preparation and characterization of Mucoadhesive nanoparticles by using chitosans, sodium alginate as mucoadhesive materials. Optimization was done by *in vitro* drug release and Mucoadhesive washout test.

Keywords: Ranitidine, Chitosan, PDI, Antagonist.

[1 2] Department Chemistry, [1] Christu Jyothi Institute of Technology & Science, Jangaon, Telangana – India,
[2] Chaitanya Postgraduate College, (Autonomous) Warangal, Telangana - India.

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CHEMISTRY RESEARCH A RTICLE

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Jagadeesh Kumar Ega [1] , Kavitha Siddoju [2]*

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ABSTRACT

Ranitidine Hydrochloride is pale yellow, Granular substance Soluble in water, Histamine 2-receptor antagonist and antiulcer drug. In this paper we have evaluated the drug Ranitidine Hydrochloride by Release kinetics , *In vitro* release studies ,Morphology , Poly dispensability index (PDI) , Drug entrapment efficiency And Zeta potential . The present's investigations mainly focus on preparation and characterization of Mucoadhesive nanoparticles by using chitosans, sodium alginate as mucoadhesive materials. Optimization was done by *in vitro* drug release and Mucoadhesive washout test.

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1. INTRODUCTION

Mucous membrane is the main administration site for bioadhesive systems. The mucous site most used for drug administration and absorption is gastrointestinal· Bioadhesive systems applied to mucous membrane are frequently defined as mucoadhesive .Bioadhesion can be defined as the state in which two materials, at least one of which is biological in nature, are maintained together for a prolonged time period by means of interfacial forces.

Control particle size, control surface properties, control release of pharmacologically active agents, And in order to achieve the site-specific action at therapeutically optimal rate and dose regimen. Achieve both passive and active drug targeting. Drug therapeutic efficacy, Reduction in side effects, controlled release and sustain release, site-specific targeting also discussed.

A mucoadhesive nanoparticle delivery system was envisioned for DTZ as such a system when administered would adhere on the gastric mucosa for a prolong period of time and the drug would be available at the main site of absorption. As tumor architecture causes nanoparticles to preferentially accumulate at the tumor site, their use as drug delivery vectors results in the localization of a greater amount of the drug load at the tumor site, to polymeric nanoparticle chemistry, research has quickly been directed at multi-functional nanoparticles, tumour therapy and tumor imaging in an all-in-one system providing a useful multi-modal approach in the battle against cancer.

2. EXPERIMENTAL SECTION

The experimental work consisted Selection and collection of raw materials, Construction of calibration curve of Ranitidine hydrochloride. Drug and polymer interaction studies by FTIR. Preparation of Mucoadhesive nanoparticles containing Ranitidine hydrochloride by the Double emulsification-solvent evaporation method.

Preformulation testing is the first step in the rationale development of dosage forms of drug substance. It can be defined as an investigation of physical and chemical properties of drug substance alone and when combined with excipients. The overall objective of preformulation testing is to generate information useful to the formulator in developing stable, efficacious and safe dosage form.

Mucoadhesive nanoparticles of ranitidine hydrochloride were prepared by type double emulsification-solvent evaporation technique. Required quantity of drug (Ranitidine hydrochloride) was dissolved in suitable solvent

(water). Required quantity of polymeric solution was prepared (chitosan in 0.25% acetic acid and sodium alginate in water). The drug solution was added slowly to the polymeric solution and then homogenized for 15 mins in ultra-probe sonicator. During sonication Tween 80 and Glutaraldehyde was poured. The resultant primary emulsion was poured into 2% poloxamer 407 solutions and homogenized for an additional 10 mins; w/o/w emulsion was formed. The solvent was removed by evaporating in a Rota vapor. The emulsion was freeze-dried at -20 ^{0}C to get dried mucoadhesive nanoparticles.

3. EVALUATION OF NANOPARTICLES

Morphology of Nanoparticle was observed by Scanning Electron Microscope. A small amount of nanoparticle samples was spread on a metal stub. The stub was then coated with conductive gold by Hitachi 1010 ion sputter and was examined under Hitachi 3000N scanning electron microscope (JSM 5610 LV SEM, JEOL, Japan) chamber. The image was photographed at an acceleration voltage of 20 kV with a chamber pressure of 0.6 mmHg. Nanoparticles size was determined using a Zetasizer 300 HS (Malvern instruments UK). Samples were diluted with distilled water and measured at a temperature of 25 ºC. The diameter was calculated from the autocorrelation function of intensity of light scattered from nanoparticles. The Particles measured are in triplicate.

4. RESULTS AND DISCUSSION

On the basis of preliminary identification test it was concluded that the drug complied the preliminary identification. By scanning the drug in U.V spectrophotometer in 200-400 nm range, a sharp peak was observed at 313nm using distilled water as solvent. It was concluded that the drug has λ_{max} of 313nm.

The morphology and surface characters of ranitidine hydrochloride mucoadhesive nanoparticles were observed by SEM. The scanning election micrographs of mucoadhesive nanoparticles of chitosan, sodium alginate were shown in figures respectively, which revealed the formation of spherical shape with smooth surface. However, chitosan mucoadhesive nanoparticles (F1- F6) showed large population of small particles. Sodium alginate mucoadhesive nanoparticles (F7-F12) had relatively smaller with rough and irregular surface.

The particle size of prepared Ranitidine hydrochloride mucoadhesive nanoparticles was analyzed by Malvern particle size analyzer. All the formulations size range between 110± 0.8 to 180.6 ± 2.2nm (F1-F6). These sizes of mucoadhesive nanoparticles were only used to improve the mucoadhesive delivery of Ranitidine. The effect of polymer type and concentration on the particle size of mucoadhesive nanoparticles [F1-F6] was investigated. In the case of F1, F2, the observed particle size was of 116.2 nm, 124.0 nm respectively. In the case of F3, F4 the chitosan mucoadhesive nanoparticles particle size was 108.8nm and 110.6nm. But in case of F5, F6, the results showed huge variation of 110nm, 180.6nm respectively. Similarly has reported that the particle size of mucoadhesive nanoparticles increased with increase in polymer concentration from 9.5 to 18%.

The Polydispersity index value of Ranitidine hydrochloride mucoadhesive nanoparticles formulation was 0.06 to 0.7**.** In case high value of F3, F4, could be due to high viscosity of mucoadhesive nanoparticles dispersion, which could affect the homogenization efficiency and resulted in a monodispersed particle size distribution. The small particles of Ranitidine hydrochloride mucoadhesive nanoparticles formed by chitosan containing preparations. The particle size of nanoparticles was the main factor for permeation through membrane. Particles size of 20-200nm were easily transported via layers by passive diffusion, whereas particles size of Ranitidine hydrochloride mucoadhesive nanoparticles formed were in the range of 108.8 nm to 124nm, which significantly increases the penetration through epithelia and intracellular penetration into the inner layer of mucus membrane.

The FTIR studies showed that the significant peaks of Ranitidine hydrochloride where C-N stretching at 1444.02 cm-1, C=O cm^{-1} vibration at 1682.16 cm^{-1} ,C-O-C at 1085.35 cm^{-1}, N-H cm^{-1} at 3301.77 cm$^{-1,}$ C=C group vibration at 1630.68 cm^{-1} and O-H vibration at 2799.45 cm^{-1}**.** Based on that FTIR spectrum of Ranitidine functional groups peak was coincided with standard Ranitidine pure drug. Based on this result the drug was confirmed as in its pure form without by-products

5. CONCLUSION

In the present investigation, me discussed about ranitidine hydrochloride mucoadhesive

nanoparticles using various mucoadhesive agents like chitosans sodium alginate .ranitidine is a antiulcer drug which mainly acting on GIT parietal cell and reduces she secretions of gastrin and acetylcholine. The conventional formulations had less action on parietal cells due to more wash off period. The problem was rectified by made as mucoadhesive nanoparticles of ranitidine by double emulsifications method.

The prepared mucoadhesive nanoparticles have satisfied physiochemical parameters like particle size, PDI, EE (%) and zeta potential .In these above parameter chitosan based nanoparticles formulation (F5) showed very significant entrapment efficiency and narrow particle size case sodium alginate based formulations (F11) showed satisfied report. Further, it was supported by *in vitro* drug release and wash off test of above two formulations (F5&11).

From the above formulations, sodium alginate based formulation has (F11) showed sustained effect as well as good initial burst release compared to chitosan based mucoadhesive nanoparticles. From the above discussion, we conclude that mucoadhesive nanoparticles can showed satisfied action as treatment of ulcers for prolong release. Further, the research will proposed to extend an animal studies in future.

Finally the FTIR studies of mixture of polymers and drug does not show any significant change. These results indicate that there is no interaction between drug and Selected polymers. The compatibility studies of polymer and drug reveals the entrapment efficiency of drug in the polymer. If incompatibility occurs between drug and polymer, lead to cross liking in polymer, which reduces the drug entrapment.

Table. 1 List of chemicals

Chemical name	Source
Ranitidine hydrochloride	Yarrow chemical product, Mumbai.
Tween 80	Merck specialities pvt ltd, Mumbai.
Sodium alginate	Nice chemicals pvt ltd, cochin.
Chitosan	Finar chemical limited, Ahmadabad.
Glutaraldehyde	Finar chemical limited, Ahmadabad
Poloxamer	Burgoyne Burbidge's &co, Mumbai.

Table .2 List of equipment's

Equipment	Source
Digital weighing balance	Systronics, India
Bath sonicator	Ralsonics model, Mumbai
UV spectrophotometer	Systronics, India
FTIR	Brucker, Japan
Optical microscope	Dolphin
Magnetic stirrer	Remi eguipments pvt.ltd.

Figure.1 scanning election micrograph of F5 formulation

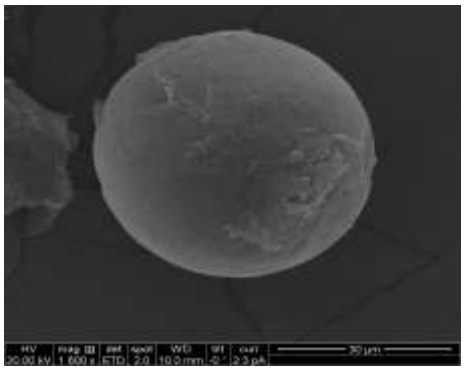
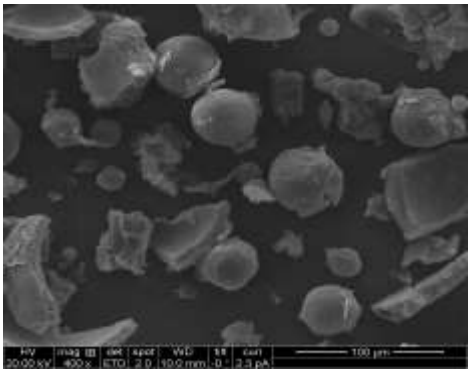


Figure.2 scanning election micrograph of F11 formulation



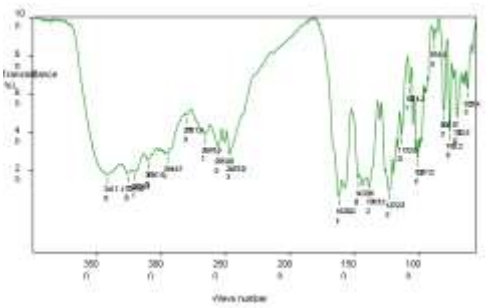


Figure 3- FTIR spectra of Ranitidine hydrochloride

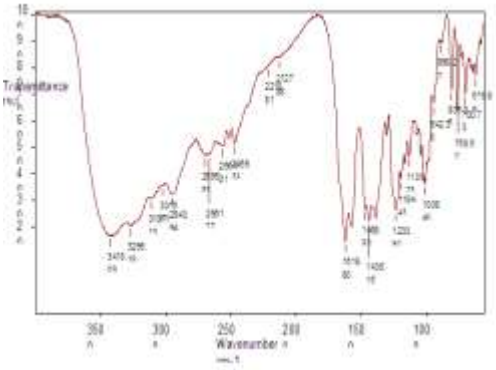


Figure 4- FTIR spectra of Ranitidine hydrochloride with chitosan

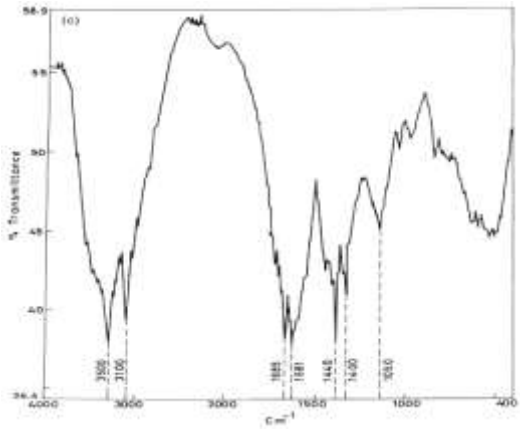


Figure 5- FTIR spectra of Ranitidine with sodium alginate

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