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FORMULATION DEVELOPMENT OF MUCOADHESIVE MICROSPHEREs

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ABSTRACT

One of the most popular drug delivery methods is oral since it is less expensive, simpler to administer, and results in improved patient compliance. This delivery system's primary issue is incorrect medication absorption, which results in subpar efficacy. The drug's lower bioavailability is caused by its limited therapeutic absorption window, which prevents it from being absorbed at the absorption site for long enough. Intimate contact between the drug delivery system and the absorbing stomach mucosal membrane is provided by gastroretentive drug delivery systems, which enhances the therapeutic effectiveness of the drug and can extend the time between doses. The goal of the current work study was to create gastroretentive mucoadhesive amoxicillin microspheres using the spray drying method. These microspheres adhere to the gastric mucosa and release the medication over a longer period of time, reducing fluctuations in drug concentration and requiring lower doses and less frequent dosing. It can be said that Box-Behnken design was successfully used in the creation and improvement of mucoadhesive microspheres of amoxicillin. The carbopol 971P, HPMC K15M, and spray drying techniques were used to create the gastroretentive mucoadhesive microspheres of amoxicillin that can be administered in sachet packaging. With mucoadhesion of 82% up to 6 hours, the mucoadhesive microspheres created in the present investigations demonstrated consistent drug release over 8 hours.

Keyword amoxicillin, microsphere, spry dryer Mucoadhesive.

INTRODUCTION

Drugs delivered by gastroretentive drug delivery systems spend more time in the stomach and proximal small intestines, increasing their gastric residence time. The bioavailability of the medicine increases, drug waste is decreased, and the solubility of drugs that are less soluble in the gastric environment is improved by the longer time the drug spends in the stomach. It offers local drug delivery to the colon and gastric regions.The amount of time that the medications may be released is important. In addition to extending dosing intervals, they also improve patient compliance beyond what is possible with currently available controlled release dosage forms. The two main drawbacks of conventional oral controlled dose formulations are uncertain gastric emptying time and brief gastric retention duration.

The condition in which two materials, at least one of which is biological in nature, are kept together for a long time by interfacial forces is known as mucoadhesion. It is possible to extend the gastro retention time of drug delivery systems (DDS) by using mucoadhesive delivery systems, which adhere to the surface of mucosal cells of mucin or gastric epithelia and increase the therapeutic result as well as the contact time with the biological membrane12. A mucus lining or biological membrane of the GI mucosa can be adhered to by a natural or synthetic polymer acting as a mucoadhesive material. This adhesive relationship can be mediated

via bonding, hydration, or receptors. When hydrated, hydrophilic polymers that are involved in hydration-mediated adhesion adhere, demonstrating mucoadhesion. Chemical or mechanical bonding is involved in adhesion that is mediated by bonds. Between certain polymers and specific receptors articulated on gastric cells, receptor-mediated adhesion arises.

The contact stage and the consolidation stage are the two key stages that make up the mucoadhesion mechanism.

step of contact: During this step, the dosage form comes into touch with the mucoadhesive on the mucous membrane, which causes the mucoadhesive formulation to disperse and swell before allowing the medicine to be released at the targeted site.

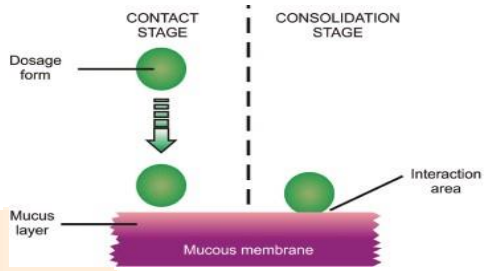

Fig.: Mucoadhesion mechanism

Consolidation stage: During this phase, moisture activates the mucoadhesive substance, which is then coupled by two forces—basically weak van der Waals forces and H+ bonds—before the material separates. This stage mostly includes two theories. Convection theory and Theory of dehydration

FORMULATION

Amoxicillin serves as the primary medication in the gastroretentive microspheres, which are then encased in the polymers carbopol 971P, which delays release, and HPMC K15M, which gives the microspheres mucoadhesiveness. The factorial design technique was used to optimise the formulation of mucoadhesive microspheres.Spray drying was used to create microspheres that were loaded with amoxicillin. Dichloromethane was continuously stirred while HPMC K15M was dissolved therein. In methanol, carbopol 971P and amoxicillin were dissolved. HPMC solution was stirred while methanol solution containing the medication and carbopol 971P was added. Using a magnetic stirrer, the finished solution was subsequently agitated for an additional 10 minutes. The product was then collected after this solution was sprayed using a spray drier. Below is a description of spray drying parameters:

Parameters	Specification
Inlet temperature	120°C
Outlet temperature	60°C
Feed rate	20 RPM (rotations per minute)
Atomization pressure	0.2 MPa (Mega Pascal)
Aspirator pressure	-100 mmWc

Table Spray Drying Parameters

10 mg of microspheres that had been precisely weighed were added to a 10 ml volumetric flask with an appropriate amount of methanol, and the volume was brought to 10 ml with 0.1N HCl and sonicated for 10 minutes. The sample was appropriately diluted before being examined using a Shimadzu UV-1700 at 278 nm. The optimised microsphere formulation's entrapment effectiveness was found to be 92%.

morphology

Scanning electron microscopy was used to examine the morphological traits of optimised microspheres. On a metal stub, a few microspheres were scattered. The sample-containing stub was then put inside the JSM 5600 scanning electron microscopy chamber (JOEL, Japan). At varied magnifications and an acceleration voltage of 20 KV, scanning electron photomicrographs were taken.

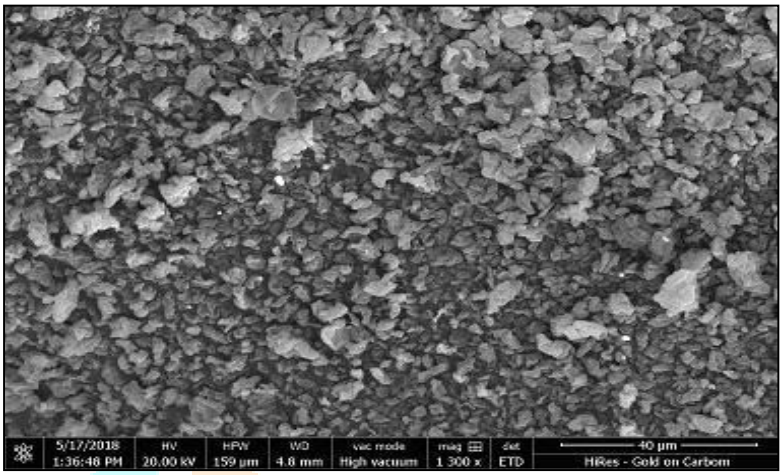

Fig.: Image of an improved microsphere taken using scanning electron microscopy

Ex-vivo mucoadhesion study

In order to determine the mucoadhesive strength of the microspheres ex-vivo mucoadhesion test was conducted. A strip of goat stomach mucous membranes (3cm long and 1cm wide) was attached on a glass slide and accurately weighed microspheres (50 mg) were spread uniformly on the surface of intestinal mucosa. Mucosa with microspheres was placed in a chamber (90% relative humidity and roomtemperature) for 20 minutes to allow the hydration of microspheres. Glass slide was taken out and fixed at an angle of 45°C. The mucosal surface was rinsed with 0.1 N HCl using syringe pump (Top Company, model 5300) at a flow rate of 1 ml/minute. Washings were collected, centrifuged (Eppendorf Company, Minispin) for 7000 RPMfor 15 minutes and dried.

In-vitro drug release data

In-vitro drug release study was conducted using USP apparatus-I, Electrolab (basket-type dissolution apparatus). Study was carried out using 0.1N HCl as a dissolution medium. In this study, 10 mg drug loaded microspheres were transferred into basket and experimental conditions are provided in table . At predetermined time intervals samples are withdrawn and filtered through 0.45µ membrane filters and analyzed at 278 nm. The results for in-vitro release studies are reported in table 31and graphically represented in fig.

Table Description of in-vitro drug release study

Parameters	Description
Speed of rotation	50 RPM
Media	0.1N HCl
Media temperature	37°C ± 0.5°C
Media volume	900 ml
Sampling points	15,30, 60, 120, 240, 360 and 480 minutes

Table : In-vitro release profile

S.No.	Time interval (min)	% Cumulative drug release
1	15	30.8
2	30	36.36
3	60	45.18
4	120	57.26
5	240	64.44
6	360	72.99
7	480	74.87

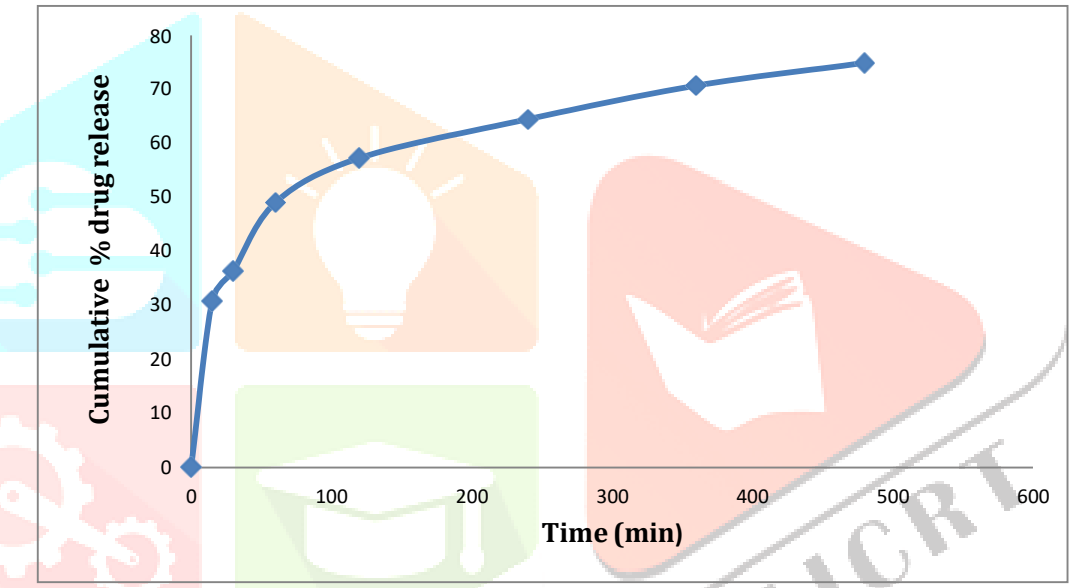

Fig. Release profile of optimized batch of mucoadhesive microspheresInference: Drug release profile showed that drug released for 8 hours constantly.

CONCLUSION

Gastroretentive microspheres stay in the gastrointestinal area for a longer duration by sticking to the mucosal membrane. Thus, a single dose of amoxicillin reduces the need for numerous doses, improving patient compliance. The goal of the current study was to create amoxicillin gastroretentive mucoadhesive microspheres using spray drying, which would release the medication for a longer period of time in the gastrointestinal region.

The amoxicillin sample used in the current research was a mucoadhesive microsphere formulation. Particle size distribution, drug content, and percent cumulative drug release at 15, 30, 60, 120, 240, 360, and 480 minutes were chosen as response factors for optimisation experiments, whereas amoxicillin concentration, carbopol 971P, and HPMC K15M were chosen as independent variables. The experiments' results were statistically examined for response factors. For each response variable, response surface graphs, contour plots, and 3D contour plots were created and examined. The most desirable formulation of the software's suggested formulations (CTMM-1 to CTMM-15) was chosen to become the optimised microsphere formulation of amoxicillin (OP-CTMM). Finally, amoxicillin mucoadhesive microspheres were created and

experimentally verified utilising the predicted optimised recipe. The optimised batch's in-vitro drug release research revealed a constant drug release lasting up to 8 hours.

In summary, it can be said that Box-Behnken design was successfully used in the creation and improvement of mucoadhesive microspheres of amoxicillin. The carbopol 971P, HPMC K15M, and spray drying techniques were used to create the gastroretentive mucoadhesive microspheres of amoxicillin that can be administered in sachet packaging. With mucoadhesion of 82% up to 6 hours, the mucoadhesive microspheres created in the present investigations demonstrated consistent drug release over 8 hours.

The developed gastroretentive mucoadhesive microsphere can therefore be used as a potential drug delivery system, which is expected to provide antibacterial activity with longer residence time in the gastric region by adhering to gastric mucosa and enhance the bioavailability of amoxicillin. This conclusion was reached based on the aforementioned findings and results.

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