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RESEARCH ARTICLE

FORMULATION AND IN-VITRO EVALUATION OF MUCOADHESIVE TABLET OF FAMOTIDINE.

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Abstract

Famotidine is a histamine H2-receptor antagonist. It is widely prescribed in active duodenal ulcers, gastric ulcers, Zollinger-Ellison syndrome, gastroesophageal reflux disease, and erosive esophagitis. The effective treatment of erosive esophagitis requires administration of 20 mg of Famotidine 4 times a day. a conventional dose of 20 mg can inhibit gastric acid secretion up to 5 hours but not up to 10 hours. An alternative dose of 40 mg leads to plasma fluctuations; thus, a sustained release dosage form of famotidine is desirable. The short biological half-life of drug (2.5-4 hours) also favors development of a sustained release formulation. The present study aims to reduce the dosing frequency by using single and combinations of synthetic and natural polymers for preparation of mucoadhesive tablets. Various approaches to combine synthetic (HPMC-K4M, SCMC and sodium alginate) and natural (tragacanth and acacia) hydrophilic polymers have been made to prepare total eight formulations. Further, these formulations were subjected to different evaluation studies like friability, content uniformity, surface pH, wash-off and dissolution tests. All the tests were performed using standard methods. Results for in vitro drug release and wash-off studies suggest that the formulation (FHT) containing HPMC-K4M and tragacanth has shown better mucoadhesive property. Other studies have shown satisfactory results in all eight formulations. Thus, the present investigation suggests the combination of HPMC-K4M and tragacanth, as hydrophilic polymers for preparation of famotidine mucoadhesive tablets.

Introduction:-

The oral route of drug administration is the most convenient and commonly used method of drug delivery. However, this route has several physiological problems, including an unpredictable gastric emptying rate that varies from person to person, a brief gastrointestinal transit time and the existence of an absorption window in the upper small intestine for several drugs [1]. These difficulties have prompted researchers to design a drug delivery system which can stay in the stomach for prolonged and predictable period attempts are being made to develop a controlled drug delivery system, which can provide therapeutically effective plasma drug concentration for a longer period, thereby reducing the dosing frequency and minimizing fluctuations in plasma drug concentration at steady-state by delivering the drug in a controlled and reproducible manner. Mucoadhesive drug delivery systems are delivery systems which utilized the property of bioadhesion of certain polymers which become adhesive on hydration and

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hence can be used for targeting a drug to particular region of the body for extended period of time [2]. Mucoadhesion was defined as the state in which two materials, at least one is biological in nature, held together for an extended period of time by interfacial forces alternately it was defined as the ability of a material synthetic or biological to adhere to a biological tissue for an extended period of time. Mucoadhesion is a field of current interest in the design of drug delivery systems. Mucoadhesive drug delivery system prolong the residence time of the dosage form at the site of application or absorption and facilitate an intimate contact of the dosage form with the underline absorption surface and thus contribute to improved and or better therapeutic performance of the drug. Famotidine is an H2 (histamine)-receptor antagonist, also known as an H2-blocker. Histamine is a chemical in some cells of the body that causes production of acid in the stomach. H2-blockers inhibit histamine action, and therefore reduce gastric secretion or the amount of acid produced. Magnesium hydroxide and calcium carbonate are both antacids that function by neutralizing excess gastric acid.

Materials and Methods:-

Famotidine (Balaji drug supplier surat, Gujarat), HPMC, Sodium carbonate, Magnesium striate (Subhampharma chem. Mumbai), Steric acid, Sodium carbonate, Xanthum gum, Citric acid, Talc (Pargati chem. Impact PVT. LTD. Mumbai) were employed in the present study. All other chemicals were of analytical grade and were freshly prepared.

Method of preparation of famotidine mucoadhesive tablet: -

Mucoadhesive tablets each containing 20 mg of Famotidine were prepared by conventional wet granulation method employing HPMC-K4M, SCMC, sodium alginate, acacia and tragacanth as mucoadhesive materials [3,4]. A batch of 100 tablets was prepared in each case a blend of 2 gm of famotidine with required number of polymers and required amount of diluents which were then granulated along with a solvent blend of water and ethyl alcohol (1:1). At first the required quantity of drug, diluent and polymer taken in a motor and pestle for trituration. Then the solvent is added drop wise with continuous stirring until the wet mass is formed. Then the wet masses were passed through 12 mesh sieve and wet granules were dried at 60º C for 4 hours. The dried granules (20 mesh) after blending with talc (0.1 gm) and magnesium stearate (0.1 gm) in a laboratory cube blender for 5 mins were compressed into 100 mg tablets of hardness 7-8 kg/sq.cm on a tablet compression machine. The tablets were then considered for further study [5,6,7].

Evaluation of mucoadhesive formulation [6, 7]:

The physical evaluation tests for the mucoadhesive tablets of all the formulations were performed and mean values were calculated. Weight variation analysis was done by weighing 20 tablets individually, the average weight was calculated and % variation of each tablet from the average weight of tablets was calculated. Hardness and friability of the mucoadhesive tablet formulations were evaluated using Monsanto hardness tester and Roche friabilator respectively.

Bulk density:

Bulk density was determined by pouring the blend into a graduated cylinder. A quantity of 10 g of powder from each formulation, previously lightly shaken to break any agglomerates formed was introduced into a 50 ml measuring cylinder. The bulk volume and mass of the powder was determined. The bulk density was calculated by using below mentioned formula. The result is given in following table.

Drug Content uniformity:

The tablets were kept in 100 ml volumetric flask containing phosphate buffer pH 4.5 for 24 h. When tablets were completely dissolved the solution was centrifuged. After centrifuged the supernatant was collected. Absorbance was measured spectrophotometrically at 267 nm. Dilution was made using phosphate buffer (pH 4.5) as per requirement.

In vitro buoyancy determination:

The in vitro drug release study was performed using USP dissolution rate test apparatus (paddle type; 50 rpm). Dissolution study was carried out for 12 h. Phosphate buffer (pH 4.5; 900 ml) was used as dissolution media. Samples of each 5 ml were withdrawn after every 1 h for a period of 12 h. Volume in dissolution vessel was kept constant by equal replacement with fresh media. The samples were collected in test tubes after filtration through Watt Mann filter paper. The amount of the drug in the aliquots was quantified by taking the absorbance of the sample at 267 nm spectrophotometrically, using phosphate buffer pH 4.5 (dissolution media) as the blank. The

formulation of F1 to F4 buoyancy lags time (sec.) between 4.5 to 5.5 sec. and total adhesive time (hr) 10 to 12 hr. or more.

Result and discussion:-

The prepared mucoadhesive tablets were evaluated for various physical parameters such as weight variation, hardness, friability and drug content. All the batches were produced under conditions to avoiding processing variables. Hardness of tablets ranged from 3.5 to4.5 kg/cm^2 and the percentage friability was between 0.4 to 0.5% as shown in **table no 2**, is within limit of IP. The values of hardness test and percentage friability indicates good handling property of prepared mucoadhesive tablets. The percent drug content of formulation F1 to F4 was found to be 92.18 to 95.37%as shown in **table no 2**. The release of famotidine from the prepared formulations was analyzed by plotting cumulative percentage drug release vs time as shown in **figure 1**. In the present study the formulation famotidine. F1-F4 was 68.75%, 65.63, 69.7, 72.66, 81.65% respectively. The batch F4 shows highest release of drug among the all batches as shown in **figure 1**.

Table No.1:-Formulation codes of different famotidine mucoadhesive tablets

Formulation code	F 1(mg)	F 2(mg)	F 3(mg)	F 4(mg)
Famotidine	20	20	20	20
HPMC 100	---	80	100	80
Xanthum gum	100	----	20	40
Sodium bicarbonate	60	60	50	50
Lactose	45	65	45	45
Steric acid	30	30	30	30
Magnesium stearate	3	3	3	3
Citric acid	40	40	30	30
Talc	2	2	2	2

Table 2:-Evaluation of famotidine mucoadhesive granules

Formulation	Tablet hardness	Tablet friability	Drug content uniformity
F1	4.0	0.532	94.10
F2	4.5	0.658	95.37
F3	3.5	0.498	92.18
F4	4.0	0.456	95.00

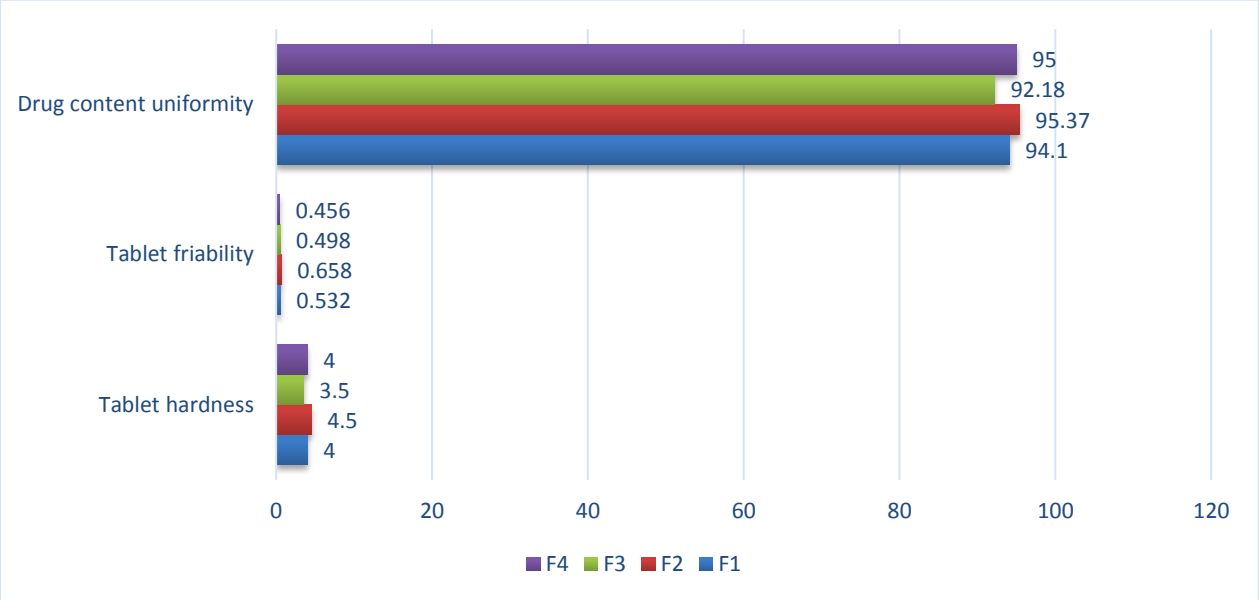

Figure 1:-% Cumulative drug release of mucoadhesive tablet of Famotidine

Conclusion:-

Formulation F_1 the value for the angle of repose was found this indicates good flow property of powder the bulk density and tapped density the powder is indicates the powder is not bulky. Formulation F_2 the value for the angle of repose was found to be 24. This indicates good flow. Flow property of powder the bulk density the powder tapped density the powder is indicates the powder is not bulky. Formulation F_3 the value for the angle of repose was found to be 20. This indicates good flow. Flow property of powder the bulk density the powder tapped density the powder 0.598 is indicates the powder is not bulky. Formulation F_4 the value for the angle of repose was found this indicates good flow. Flow property of powder the bulk density the powder and tapped density the powder is indicates the powder is not bulky.

The entire formulation tablet F1 to F4 passed the weight variation test as the percent weight variation was within the pharmacopeia limit of 5% of average weight.

The thickness of mucoadhesive tabets were measured by screw guaze of formulation F1 to F4 and were good range. The hardness of the mucoadhesive tablet was measured by the monosanto tester of formulation F1 to F4 and were controlled, the standard hardness of the tablet is 4 kg/cm^2.The friability of the mucoadhesive tablet was measured by the roches fribiliter of formulation F1 to F4 and were controlled the standard friability of the tablet is below 0.8% according to IP and 1% according to USP.The percent drug content of formulation F1 to F4 was found to be of famotidine which was within the acceptable limit, the standard drug content uniformity 100±10%The formulation of batches of mucoadhesive tablet of famotidine F1-F4 was respectively. The batch F4 shows highest release of drug among the all batches.

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