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FORMULATION AND EVALUATION OF FUROSEMIDE TABLETS UTILIZING EXTRACTION OF MUCILAGE OF OLIBANUM FOR ENHANCED DRUG DELIVERY

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ABSTRACT

Furosemide, a commonly used diuretic, presents difficulties due to its solubility and effectiveness, requiring creative administration methods. Olibanum mucilage, obtained from Boswellia trees, has mucoadhesive and film-forming characteristics that are suitable for medicinal uses. The study included extracting mucilage from Olibanum obtained from Boswelliaserrata using a maceration procedure with water and chloroform. The mucilage was then precipitated using 100% ethanol, resulting in a yield of 40% w/w. Mucilage was used in varying percentages of 5%, 7%, and 10% w/v. The granules were produced using the wet granulation method. The granules were assessed for fines percentage, average particle size, total porosity, compressibility index, and flow characteristics. The qualities were compared with starch, which served as the standard binder at a concentration of 10% w/v. The tablets were formulated and assessed for consistency in content, hardness, fragility, disintegration time, and dissolving behavior in a laboratory setting. Therefore, 5% and 7% concentrations are optimal for preparing Furosemide tablets.

Keywords: Furosemide, Olibanum, Mucilage, Granules, Gum

I.INTRODUCTION

The powerful diuretic furosemide is a prime example of a medication that requires novel delivery methods to improve its pharmacokinetic profile and therapeutic effects; it is extensively used to treat hypertension, congestive heart failure, and edema caused by renal dysfunction. Using mucilage made of Olibanum, or frankincense, as an excipient is a potential way to improve formulation and increase drug delivery efficiency in this setting. Furosemide tablet formulation and assessment is an important pharmaceutical research activity because it tries to solve problems with the drug's solubility, dissolution kinetics, therapeutic efficacy, and bioavailability. An interesting possibility in this area is to use Olibanum mucilage, which has natural qualities that may improve the bioavailability, therapeutic effectiveness, and drug release kinetics of furosemide tablets.

The medicinal and therapeutic attributes of olibanum, which is extracted from Boswellia tree resin, have been highly esteemed for ages. The mucoadhesive, film-forming, and swelling capabilities of Olibanum mucilage, which is rich in polysaccharides and terpenoids among other bioactive components, make it an ideal ingredient for pharmaceutical formulations. Researchers want to use Olibanum mucilage's unique qualities to solve the problems with traditional furosemide formulations and find novel ways to improve medication delivery by using these traits.

Olibanum mucilage's ability to control disintegration, solubility, and penetration across biological barriers is the basis for its use into furosemide tablets. Olibanum mucilage’s mucoadhesive characteristics make it easy for the tablet to stick to the gastrointestinal tract’s mucosal surfaces, increasing furosemide’s residence time and absorption. Also, Olibanum mucilage's film-forming

properties allow for drug rate modulation, leading to prolonged or controlled release patterns that are specific to therapeutic needs.

Olibanum mucilage is a pharmaceutical excipient that fits the bill since it is biodegradable and compatible with human bodies, which is in line with the current trend in pharmaceutical research toward more environmentally friendly and sustainable formulation methods. Researchers are leveraging natural materials like Olibanum mucilage to generate pharmaceutical solutions that are greener and more ecologically sustainable. This helps alleviate worries about the toxicity and bad effects of manufactured excipients.

A thorough review of many physicochemical, pharmacokinetic, and pharmacodynamic characteristics is of utmost relevance when aiming to optimize furosemide distribution with Olibanum mucilage-based formulations. Successful tablet formulations may be developed when the extracted mucilage is characterized, which involves testing its rheological characteristics, molecular composition, and compatibility with furosemide. Disintegration time, dissolving profile, pharmacological activity, and drug release kinetics are some of the essential properties that may be evaluated by subsequent in vitro and in vivo research. These studies provide vital insights into the performance and therapeutic potential of the manufactured tablets.

II.REVIEW OF LITERATURE

Salomy, A et al., (2020) Patient compliance, convenience of administration, correct dose, self-medication, and pain avoidance are the most significant reasons for the popularity of solid dosage forms. Among the several solid dosage forms for oral administration, fast-dissolving tablets have become more important. Not only are they great for energetic persons, but they are also recommended for those who have trouble swallowing. Within minutes of placing the dose form in the mouth, it will dissolve and disintegrate, eliminating the need for water or chewing. Advantages include stability, quick start of action, enhanced bioavailability, quick absorption via pre-gastric absorption of oral medications, and quick absorption overall. Because of this, the bioavailability of the medications is much higher than it would be with the traditional tablet dose form. We will be using furosemide, a powerful loop diuretic, in this trial. Because of first-pass metabolism, its oral bioavailability ranges from 43% to 69%. Formulating it into fast-dissolving tablets may boost its bioavailability by bypassing first-pass metabolism. The direct compression technique, in conjunction with super disintegrants, is used to make furosemide fast dissolving tablets. Here, super disintegrants of 5%, 5.6%, and 6.4% sodium starch glycolate, crospovidone, and croscarmellose, respectively, are used. Research on medicine authenticity, repose angle, bulk density, tapped density, compressibility index, and hausner's ratio are all part of the precompression blend evaluation procedures. After compression, the mix is subjected to a battery of tests to determine its quality, including those for thickness, hardness, friability, weight fluctuation, disintegration, and in vitro dissolution. Disintegration time was shortest for formulations containing crospovidone, a super disintegrant. At the conclusion of the 10-minute time period, the 963 Diyya et al. formulation, F3, which contains 6.5% crospovidone as a superdisintegrant, demonstrated 99% drug release.

Shanmugam, S. (2017)Using natural polymers, this work aimed to create levosulpiride sustained-release matrix tablets. The tablets were made using the wet granulation process with varying ratios of chitosan, xanthan gum, and guar gum. The purpose of the levosulpiride solubility investigation was to determine an appropriate dissolve medium for the in vitro drug release experiments. The results of the Fourier transform infrared (FTIR) analysis showed that the IR peak of levosulpiride did not change significantly, indicating that the medicine did not interact with the excipients. There was no evidence of medication interaction during production, according to DSC thermograms. Each formulation underwent an in vitro dissolving investigation, with outcomes compared to those of a commercially available sustained release tablet. Matrix tablets' drug release was seen to diminish when the polymer

ratio of chitosan, xanthan gum, and guar gum increased. When tested in dissolving medium, Formulation LF3 showed a medication release profile very comparable to commercially available tablets. It was discovered that the drug release happened via a diffusion process, as the strongest correlation was shown for the First order, Higuchi's, and Korsmeyer equations, when dissolution data was fitted to several drug release kinetic equations.

Bhatia, Neelaet al., (2014) India is a country that makes extensive use of Lepidiumsativum as a natural medication. There is a large supply of it on the market, and the price is fairly reasonable. Within the context of India's traditional medical system, Lepidiumsativum has been used extensively for the treatment of a variety of diseases. The incorporation of natural gums and mucilage into the formulation process is an essential component in the production of pharmaceutical dosage forms. It is widely accepted that mucilages are typical results of metabolism that are generated inside the cell. When it comes to their therapeutic properties, mucilage and gums have been used since ancient times. Additionally, in the current period, they are used extensively in the pharmaceutical industry as thickeners, water retention agents, emulsion stabilizers, suspending agents, binders and film formers, disintegrants, as well as sustaining agents in tablets and as gelling agents. These applications are employed in a broad variety of capacities. Several components of the plant, including the seeds, the leaves, and the roots, have been used in the treatment of a wide range of patient conditions. Within the outermost layer of the seeds of Lepidiumsativum is the mucilage that surrounds the seed. Isolating mucilage presents a number of challenges, the most significant of which is that it expands but does not separate from the seeds. As a result of this, the standard techniques of mucilage separation are not relevant to the process of separating the mucilage from the seed. As a result, numerous processes were attempted in order to separate the mucilage by using a variety of approaches. In order to characterize the mucilage of Lepidiumsativum, chemical, Fourier transform infrared (FTIR) spectral, and physicochemical analyses were carried out.

Aulakh, Gurpreetet al., (2011) By virtue of its ability to connect with gastric mucus, mucoadhesive polymer extends the duration of the drug's residency in the stomach, which in turn results in an increase in the drug's bioavailability. Using myrrh oleo gum resin (MOGR), a natural mucoadhesive substance, oral controlled release mucoadhesive matrix tablets have been designed for the purpose of domperidone as a model medication in the current research.Direct compression technique was used in order to produce the tablets with the natural polymer in several concentrations, which included five, ten, fifteen, and twenty percent by weight. In vitro drug release studies, swelling index, mucoadhesive strength (using texture analyzer), and tablet parametric tests were performed on the batches that had been made. These tests included drug assay, diameter, thickness, hardness, and tensile strength. In addition, analyses of accelerated stability were carried out on each and every batch that was created. When the percentage of natural polymer is increased from 5% to 20% (M1 to M4), the tensile strength improves from 0.973±0.09 to 1.687±0.11 MN/m2, and the mucoadhesive strength increases from 19.868 to 49.778 N. Increasing the gum concentration and the time period combined led to an increase in the swelling index of natural polymer, which was evidence of the development of proliferation. Fitting in vitro release data into a variety of models and establishing that release follows zero order and the Hixson Crowell cube root law allowed for the calculation of the release kinetics as well as the mechanism of release. Due to the fact that the release exponent (n) falls within the range of 0.5889 to 0.7389, it is possible that there are numerous release processes, perhaps including a mix of erosion and diffusion. It has been shown via accelerated stability testing that there is no substantial change in the tensile strength, mucoadhesive strength, or drug assay qualities. The findings of this study make it abundantly evident that MOGR has the potential to be used in tablet formulations as a natural substance that may effectively function as a binder, release retardant, and mucoadhesive.

Awen, Bahlulet al., (2010) Using a maceration procedure that included water and chloroform, the mucilage of Oibanum was extracted from Boswelliaserrata. The mucilage was then precipitated by 100% ethanol, with a yield of forty percent and a weight-to-weight ratio.In addition to determining the microbial load, the physicochemical properties of mucilage, such as its solubility, swelling index,

loss on drying, pH, and viscosity, were investigated. Furosemide was used as a model medication in order to examine the granulating and binding capabilities of the mucilage in tablet form. Several various concentrations of mucilage were used, including 5, 7, and 10% by weight.Through the use of the wet granulation process, the granules were created. The granules that were created were examined to determine their flow parameters, which included the percentage of particles, the average particle size, the total porosity, and the compressibility index. The qualities were evaluated in comparison to starch, which served as the standard binder and was present at a concentration of 10% by weight. A variety of characteristics, including content homogeneity, hardness, friability, disintegration time, and in vitro dissolution profiles, were examined after the tablets were first manufactured. Within two hours, the tablets exhibited a drug release rate that was more than 75%, and they had favorable physicochemical features. When compared to tablets made with 5% and 7% concentrations of mucilage, those made with 10% mucilage as the binder displayed somewhat higher levels of hardness. Because of this, concentrations between 5 and 7 percent are believed to be the best values for the manufacture of tablets containing furosemide.

III. MATERIAL AND METHODS

Plant Material

The gum olibanum was sourced in its crudest form. Hyderabad, India supplied the free sample of furosemide. The research only utilized AR grade chemicals and reagents.

Isolation of Mucilage

Over the course of five days, with periodic mixing, the gum was treated with a chloroform/water combination in a ratio of 5:95. After filtering out any impurities, the gum is precipitated with the use of pure ethanol. After filtration, an ether wash, and air drying, the gum that had precipitated was removed. A 100-mesh sieve was used to powder the dried gum before it was put to another use.

Physicochemical and microbiological characterization of mucilage

The mucilage's physicochemical parameters, including its solubility, swelling index, viscosity, loss on drying, and microbiological load, were ascertained in accordance with the Indian Pharmacopoeial Procedures. An Elico® digital pH meter was used to detect the mucilage's pH.

Preparation and Evaluation of granules

As a model drug, granules were prepared using furosemide, which essentially has a weak binding characteristic. The disintegrant was starch, whereas the diluent and lubricant were lactose and talc, respectively. Mixing mucilage of gum olibanum of B. serrata with water at5,7, and 10% w/v concentrations yielded the binder solution. Granules were made using a wet granulation technique. A 250 g batch was prepared. A wet mass with enough cohesiveness was generated by gradually adding volumes of 5, 7, and 10% w/v mucilage to a powder blend that already included the drug, lactose, talc, and starch. Kneading was then carried out for 12 hours. A No. 16 sieve was used to pass the moist mixture. After that, the manufactured granules were tested for fines percentage, particle size, and flow characteristics using angle of repose measurements. Granules were evaluated for their bulk and tapped densities using tapped volumetric equipment. The Carr's index was used to establish the granules' compressibility index. Measuring the volume filled by the specified weight of powder and the real amount of granules collected also allowed us to establish total porosity.

Preparation and evaluation of Tablets

The tablets were crushed using flat-faced punches from a single punch machine (Cadmach®, India). One hundred tablets were made. The manufactured tablets were tested according to the criteria set forth in the Indian Pharmacopoeia for homogeneity of content, hardness, friability, disintegration time, and in vitro dissolution profile.

IV. RESULTS AND DISCUSSION

By utilizing ethanol as the mucilage-precipitating solvent, the gum of B. serrata that had been dried and coarsely powdered produced a high amount of mucilage, which was forty percent by weight. Table 1 contains a summary of the physicochemical and microbiological parameters of mucilage, which were determined. An analysis of the bacterial load and pH was performed on the mucilage that had been isolated and purified. The count of microorganisms was discovered to be lower than 120 colony forming units (CFU) per gram of mucilage during our investigation. It was determined that the mucilage had a pH of 6.8 or higher. Considering that the pH value of this mucilage is relatively close to neutral, it is possible that it is less irritating to the gastrointestinal system, and as a result, it was suited for tablets that were not coated.

Table 1: Physicochemical and Microbial Assessment of Olibanum Mucilage

Parameter (s)	**Result (s)**
Solubility	Insoluble in water and produces viscous solution. Soluble in alcohol, acetone, ether and chloroform
Swelling index	13%
Loss On Drying	9.2%
pH	6.8
Bacterial Load (No. of CFU/g of mucilage	103

The granules that were made were assessed for fines percentage, particle size, and flow characteristics, as shown in Table 2. The proportion of fines decreased as the concentration of mucilage rose. The fines percentage was somewhat higher in granules made with a 5% w/v mucilage binder. The flow quality of granules was assessed by measuring the angle of repose, which ranged from 28° to 31°. The average particle size ranged from 0.32 to 0.38 mm, which was deemed suitable for tablet production. Therefore, all the granules showed excellent flow characteristics. Table 2 shows that the bulk densities of the produced granules reduced marginally as the amounts of olibanum mucilage increased. The outcome might be a consequence of bigger agglomerates forming and a reduction in fines in the granules owing to higher concentrations of olibanum mucilage, which enhances binding to the granules. Table 2 shows that flowability decreases as the concentration of olibanum mucilage increases, as shown by the compressibility index data. All formulations exhibited satisfactory flow characteristics. The granules exhibited porosity ranging from 29.37% to 36.28%, suggesting they were loosely packed and had consistent particle sizes. This aligns with the typical pattern where a percentage porosity number below 26% suggests particles in the powder vary in size, while a value beyond 45% indicates particles in the powder are in aggregate or flocculate form. All these findings validate that the granules exhibited adequate flow characteristics, compressibility, and porosity.

Table 2: Examination of granules made with gum olibanum mucilage

Parameter	**Olibanum mucilage as binder (% w/v)**			**Starch 10% w/v**
	5	**7**	**10**	
Percentage of fines	19.86	16.30	14.27	18.19
Mean particle size (mm)	0.32	0.32	0.38	0.45
Angle of repose (o)	28o	31o	29o	28o
Loose bulk density (g/cm3 ± sd)	0.526 ± 0.03	0.528 ± 0.08	0.509 ± 0.06	0.490 ± 0.04
Tapped bulk density (g/cm3 ± sd)	0.590 ± 0.07	0.608 ± 0.07	0.569 ± 0.04	0.576 ± 0.02
Compressibility index (% ± sd)	8.21 ± 0.88	10.42 ± 0.73	11.82 ± 0.95	12.12 ± 1.20
Total porosity (± sd)	29.37 ± 2.11	34.92 ± 2.33	36.28 ± 3.35	37.51 ± 2.59

Three sets of 100 tablets were made using olibanum mucilage at concentrations of 5%, 7%, and 10% w/v. A 10% w/v solution of starch mucilage was employed as the standard binder for comparison.

The tablets were assessed for content homogeneity, hardness, friability, disintegration time, and in vitro dissolution profiles, and the findings are shown in Table 3. All tablet batches showed consistent and uniform furosemide content. The hardness of tablets rose proportionally with the higher amount of binding agent used. Tablets containing 10% w/v olibanum mucilage from B. serrata exhibited more hardness than tablets containing 10% starch mucilage, suggesting that olibanum mucilage has stronger binding capabilities than starch mucilage. The % friability results were consistent across all tablet batches made with varying quantities of mucilage. The olibanum mucilage exhibited a longer disintegration time as the concentration increased, although all values remained within the pharmacopoeial standards. The tablets disintegrated more slowly at a concentration of 10% w/v compared to those made with 10% w/v starch mucilage.

Table 3: Assessment of tablets made using olibanum mucilage as a binding agent

Property	**Olibanum mucilage as binder (% w/v)**			**Starch 10% w/v**
	5	**7**	**10**	
Content Uniformity (mg ± sd)	96.80 ± 0.41	97.88 ± 0.49	97.25 ± 0.48	98.16 ± 0.67
Hardness (kg/cm3 ± sd)	5.85 ± 0.11	6.52 ± 0.17	7.19 ± 0.13	6.65 ± 0.10
Friability (%)	0.35	0.32	0.35	0.20
Disintegration time (sec)	290	310	330	250

CONCLUSION

By incorporating Olibanum mucilage into furosemide tablets, its distinct traits such as mucoadhesive and film-forming qualities are used to control important factors that affect the release rate and absorption of the medicine. Moreover, using Olibanum mucilage supports the increasing focus on sustainability and eco-friendliness in pharmacological studies by providing a biocompatible and biodegradable substitute for synthetic excipients. The current study suggests that olibanum mucilage from B. serrata may serve as a binding agent in tablet formulations. The research investigates the possibility of finding novel natural materials that may be used as excipients in pharmaceutical formulations to replace synthetic excipients in the future.

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