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Studies on Propranolol hydrochloride floating tablets formulated with different concentrations of Aegle marmelos gum

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Abstract - This research employs Aegle marmelos gum in various ratios as a natural polymer to formulate and assess Propranolol hydrochloride floating tablets. Because of its high solubility and permeability, propranolol hydrochloride, a non-selective beta-adrenergic receptor blocker, has a restricted bioavailability. Floating tablets are intended to improve the absorption and bioavailability of drugs by staying afloat in the stomach. Aegle marmelos gum (AMG) was used as a polymer in varied ratios to create distinct formulations. The tablets were then tested for a number of characteristics, including hardness, friability, drug content, in vitro buoyancy, and drug release profiles. The findings showed that the Aegle marmelos gum content had a major impact on the tablets' floating qualities and drug release characteristics.

Keywords - Propranolol HCL, floating tablets, Aegle marmelos gum

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INTRODUCTION

Because natural biopolymers offer so many benefits over synthetic polymers, researchers have been using them more and more in recent years. The preferred materials are polysaccharide gums since they are nonimmunogenic, biocompatible, biodegradable, and plentiful in nature [1].

The fruit of the native Indian plant Aegle marmelos, which is a member of the Rutaceae family, is used to make gum. The scarlet, fully ripe fruit pulp has an astringent, mucilaginous flavour. Carbs, proteins, vitamins C and A, angelenine, marmeline, dictamine, O-methyl fordinol, and isopentyl halfordinol are all present in the pulp [2]. The neutral oligosaccharides, which include the acidic oligosaccharides, were identified as 3-0-beta-D-galactopyranosyl-D-galactose, 5-0-beta-D-galactopyranosyl-L-arabinose, and 3-0-beta-D-galactopyranosyl-D-galactose [3, 4].

Studies have shown that the use of gastroretentive technology may alleviate the issues related to regulated drug delivery from solid oral dosage forms that have been previously mentioned [5]. The technique greatly increases the dose form's GRT while allowing it to stay in the stomach area for a few hours [6]. Numerous methods, including hydrodynamically balanced or floating systems, swelling and expanding systems, and polymeric bio-adhesive systems, have been used to generate gastroretentive controlled release dosage forms [7]. Out of all the methods, the floating drug delivery system (FDDS) has shown to be the most effective and realistic means of attaining gastro retention. This strategy has many benefits, including increased GRT, improved medication bioavailability, and localised action in the stomach [8, 9]. Moreover, greater site-specific drug administration could be feasible because of its extended GI retention [10]. The fed state, ring or tetrahedron skeleton, diameter more than 7 mm, and the dosage form's low density in relation to the gastric medium (density less than 1 g/ml or 1.004–1.010 g/ml) are some of the factors that induce the dosage form to float on the gastric media and boost GRT [5, 11-14]. Moreover, a floating chamber that is vacuumed, vented, or filled with inert gas may be used to accomplish medication floating in the stomach [15].

A non-selective beta-receptor blocker is propranolol HCl [16]. It is used to treat both non-cardiovascular conditions such restless legs syndrome, migraines, tremors, and heart failure as well as cardiovascular conditions like coronary artery disease, heart failure, fibrillation, hypertension, and angina [17]. It falls into the BCS Class I category, takes one to three hours to achieve peak plasma concentration, and when

given orally, is totally absorbed from the GIT. If you want to establish a controlled release, this is the ideal option. FDDS because of its plasma half-life, which is around three to six hours [18]. Because of its weak basic character, which increases at lower pH values, its solubility is dependent on the medium's pH [19]. Based on FDDS, many researchers have developed formulations of propranolol HCl. A matrix approach was employed by Chaturvedi et al. to produce propranolol HCl gas floating tablets. The release of the drug was delayed by the use of HPMC K15M. Since the formulation with 27.5% HPMC delayed the release of the medicine in the stomach for a whole day, it was determined to be the best [20]. In a different investigation, Jagdale et al. created propranolol HCl gastro retentive floating tablets (GRFT). These staff members assessed the IVIV behaviour of the experimental formulations using varying doses of sodium alginate, xanthan gum, HPMC K4M, HPMC E 15 LV, and Hydroxy Propyl Cellulose (HPC). If xanthan gum was not able to manufacture tablets strong enough, it has been claimed that the tablets made with HPC and HPMC K4M controlled the release for eighteen hours [20]. Propranolol HCl floating tablets made of poly (vinyl acetate) were created. The Kollicoat SR 30D and Kollicoat IR coatings from FDDS were looked at for their ability to limit drug release. The tablets with the greatest floating strength, lowest lag time, and maximum floatability were coated with 10 mg polymer/cm2 SR/IR (8.5:1.5). Poly Vinyl Acetate (PVA) has shown itself to be an effective polymer for delaying the release of the medication from these tablets. Throughout the day, the PVA managed the drug release [20].

METHODOLOGY

A complimentary sample of propranolol HCl was provided by Saudi laboratories in Saudi Arabia. All other components, including Aegle marmelos gum, were of analytical grade.

Propranolol HCl floating tablets Preparation:

Geometric mixing was used to combine propranolol HCl with the necessary amounts of citric acid, sodium bicarbonate, and Aegle marmelos gum. Isopropyl alcohol served as the granulating fluid and PVP K 30 as the binder in the wet granulation process that was utilised to make the tablets. Talc and magnesium stearate were the glideant and lubricant, respectively, that were used. Using 12 mm punches and dies, a rotary tablet compression machine was used to crush the completed combination into tablets. Each formulation's components were mentioned in Table 1.

Table 1: Propranolol HCl floating tablets contains varying amounts of Aegle marmelos gum.

Ingredients	Propranolol HCl	Aegle marmelos gum	Micro crystaline cellulose	Sodium bicarbonate	Citricacid	Poly Vinyl Pyrolidine	Magnesium stearate	Talc	Total weight
F_1(mg)	150	75	170	50	25	20	5	5	500
F_2(mg)	150	150	95	50	25	20	5	5	500
F_3(mg)	150	225	20	50	25	20	5	5	500

Parameters of Evaluation

Granules Flow properties:

The following parameters were used to assess the granules:

- Angle of repose
- Bulk density
- Bulk density
- Carr's index
- Evaluation Parameters
- Flow properties of granules
- Hausner's ratio
- Tapped density
- Weight variation:

Propranolol HCl floating tablets Evaluation:

- Hardness:
- Weight variation
- Friability
- Swelling Index

In vitro buoyancy study:

The floating lag time and total floating duration are the characteristics of this test. 900 cc of 0.1N hydrochloric acid were used in the test, which was conducted at 37 ± 0.50 C with a paddle rotation speed of 100 rpm using a USP-Type II apparatus. "Floating lag time" and "total floating time" were the durations of time that the tablet remained

suspended in the dissolving media after it had risen to the surface.

- **Drug content:**

25 tablets were pulverised after being weighed. After dissolving the powder in 100 millilitres of 0.1N hydrochloric acid, which is equal to 150 mg of propranolol HCl, the mixture was filtered. A UV spectrophotometer was used to quantify the drug concentration, which was 5 millilitres diluted to 50 millilitres with water.

RESULT AND ANALYSIS

Propranolol HCl floating tablets were made by adjusting the Aegle marmelos gum content (F_1-F_3). Different flow characteristics of the formed granules were assessed. All of the formulations had bulk densities between 0.516 and 0.527. It was discovered that the angle of repose for each formulation fell between $25^0 41^l$-27^0 62^1. All of the formulations had Carr's indices between 15.58-14.86%. Good packing characteristics are shown by the bulk density value. For every formulation, the angle of repose (25^0-30^0) suggests a satisfactory flow characteristic. A Carr's index score between 10-16 percent implies free-flowing content. It was discovered that the values of Hausner's ratio ranged from 1.175 to 1.184. The powder mix has excellent flow qualities with a Hauser's ratio of 1.25. Thus, the results show that the granules' flow characteristics were appropriate. Table 2 presented the flow characteristics.

Table 2: Micromeritic properties of Propranolol HCl floating tablets granules formulated with different concentrations of Aegle marmelos gum content

Formulation code	F_1	F_2	F_3
Angle of repose (°)	26.72	25.9	25.41
Bulk density (gm/cm^3)	0.52	0.523	0.527
Carr's index (%)	15.58	15.23	14.86
Hausner's ratio	1.184	1.18	1.175
Tapped density (gm/cm^3)	0.616	0.617	0.619

Tablets with floating matrix were assessed for friability and hardness. It was discovered that the hardness ranged from 4.5 to 4.8 kg. Given that the tablets' percentage friability readings were less than 1%, they met the friability criteria. The estimates of drug content revealed values between 99.54 and 100.14%, indicating high consistency in drug content across various formulations. Since the weight fluctuation percentage was within the Pharmacopoeia standards of ±5% of the weight, all of the tablets passed the weight variation test. Test results for hardness, friability, and weight variation for all formulations fell within the specified ranges, indicating that the manufactured tablets are of standard quality.

Sodium bicarbonate was included in the formulation of each tablet to provide effervescence. Upon introduction to the beaker, all of the produced formulations floated immediately and maintained their floating state for over fourteen hours. The buoyant properties of the tablet were achieved by hydration of the polymer, which reduced the density (<1) and captured the carbon dioxide produced by the sodium bicarbonate in the presence of the dissolving media (0.1N HCL). Table 3 displays the results of tests on several physical parameters and invitro buoyancy.

All of the floating matrix tablet formulations underwent in vitro dissolving tests in 0.1N HCl. The 12-hour research was conducted, and the cumulative drug release was computed. For the duration of the dissolving experiments, every formulation stayed afloat and undamaged. The drug release in the formulations (F_1–F_3) including Aegle marmelos gum decreased as the gum's content increased. At 11.5 hours, the drug release from formulation F_3, which included drug and natural polymer in a 1:1.5 ratio, reached its maximum. Figure 1 displays the dissolving profile for formulations F_1–F_3, which was listed in Table 3.

Table 3: Propranolol HCl floating tablets' physical characteristics are determined by the various amounts of Aegle marmelos gum content in the formulation

Formulation	F1	F2	F3
Hardness (kg/cm^2)	4.3±0.011	4.5±0.022	4.7±0.016
Weight variation (mg)	500.23±0.13	501.12±0.18	499.66±0.23
Friability (%)	0.45±0.015	0.36±0.021	0.28±0.013
Drug content (%)	99.54±0.12	99.68±0.11	99.73±0.17
Floating (Lag time)	2.36 min	2.17 min	1.52 min
Total floating time (hrs)	>14	>14	>14

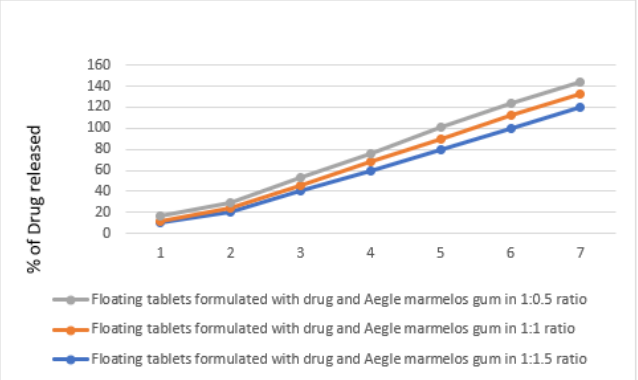

Figure 1: In Vitro drug release profile Comparative of floating tablets containing propranolol HCl and varying Aegle marmelos gum concentrations

To ascertain the drug release mechanism, the dissolution data was analysed using the Higuchi and Peppas, zero order, and first order equations. Values of the correlation coefficient (r) suggest that the drug release mechanism was directed by the Peppas model, and that the dissolution profiles

followed zero order kinetics. When n values were more than 0.5, non-fickian diffusion was the major mechanism controlling the drug release (n>0.5). Tabulated in Table 4 are the results of the in vitro drug release kinetic analysis. Table 5 displays the results of the investigations that illustrate the swelling index, which increases gradually as the proportion of natural polymers increases.

Table 4: Propranolol HCl floating tablet in vitro drug release kinetics data prepared with varying amounts of Aegle marmelos gum

	Formulation	F_1	F_2	F_3
Correlation Coefficient Value	Zero Order	0.9916	0.9951	0.9996
	First Order	0.8293	0.8058	0.7313
	Matrix	0.9524	0.944	0.9269
	Peppas	0.9963	0.9964	0.9998
Release Rate Constant (mg/hr)k_0		15.33	13.7	12.7
Exponential Coefficient (n)		0.7551	0.7976	0.973
T50	(hr)	4.9	5.5	5.9
T90	(hr)	8.8	9.9	10.6

Table 5: Propranolol HCl floating tablets formulated with different concentrations of Aegle marmelos gum concentrations: Swelling index values

		Formulation code	F_1	F_2	F_3
Swelling index	Time (Hrs)	after 1 hour	54.34	57.45	60.12
		after 2 hours	78.93	91.46	98.56
		after 8hours	149.24	157.23	171.39

DISCUSSION

It was found that the hydration of the polymer, which lowers the density (<1) and makes the tablet buoyant, captured the carbon dioxide produced by the sodium bicarbonate in the presence of the dissolving media (0.1N HCL).

The peaks in the characteristics verified propranolol HCl's structure. The drug-loaded matrix tablets all showed the same peaks. The distinctive peaks in matrix tablets did not alter or move, indicating that there was no substantial drug-polymer interaction. This suggests that the drug is stable in all formulations. At regular intervals of one month, the drug release from optimised formulations under various storage circumstances was assessed both before and after storage.

CONCLUSION

Sustained drug release has been established by the inclusion of *Aegle marmelos gum* in the formulation of Propranolol hydrochloride floating tablets. It has been shown that the floating qualities, drug release profiles, and other important aspects of the tablets are influenced by the different concentrations of the natural polymer. Selecting the ideal concentration is essential to getting the intended therapeutic result. Subsequent research avenues may include enhanced formulation optimisation, investigation of supplementary excipients for synergistic effects, and in vivo experiments to evaluate the efficacy of the tablets inside a biological system. Overall, this research offers insightful information on the creation of propranolol hydrochloride floating pills, which may improve patient adherence and treatment results.

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