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FormulationAndEvaluation ofNovel Liquorice-basedNutraceuticalFloatingTablets

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ABSTRACT

Floating pills promote the distribution of drugs to the stomach, raise the absorption of pharmaceuticals, and extend their time in the body. With this objective, For the purpose of achieving this goal, floating tablets comprising an aqueous extract of liquorice andandXanthanGum were prepared and evaluated.Floating Herbal tablets increase bioavailability, speed up local medication distribution to the stomach, and extend the duration that pharmaceuticals remain in the stomach. For the treatment of stomach ulcers, floating tablets with liquorice alcohol extract as the primary active ingredient were created in this study. The tablets containing alcoholic liquorice extract, HPMC K100M, sodium bicarbonate, talc, and magnesium stearate were made utilising the direct compression technique. The physical characteristics of the tablets, such as their diameter, thickness, hardness, uniformity of weight, and buoyancy duration, were also assessed. Formulation was improved using buoyancy time.All tablet formulations had a buoyancy time of less than 2 minutes and maintained their floating state for the duration of the research, up to a maximum of 2 hours. The formulation with the best performance, f1, had a buoyancy time of 0.25 minutes.For gastro retentive drug delivery systems, a formulation including liquorice, sodium bicarbonate, and HPMC K100M can be promising.

KEYWORDS

Nutraceutical, floating tablets, Xanthum gum, liquorice extract, gastric ulcer, floating drug deliverysystem.

Introduction

A "Nutraceutical" is an item that has been separated or refined from food and is typically sold in non-food-related therapeutic forms. A nutraceutical offers a physiological advantage or offers protection from chronic diseases [1]. Gastriculcersareusuallytriggeredbytheimbalancebetweenthequantityofacidgeneratedin the stomach and the mucous protection barrier, leading to damage stomach or duodenum mucouslining [2]. Unattended ulcers may result into severe health issues such as intestinal bleeding, intestinal liningperforation,vomitingofthebloodandobstructionofthegastricoutlet.Stomachulcersmayaffectpeopleofanyagegroup.Anestimated15,000deathsoccurbecauseofpepticulcereveryyear[3].Itisapparentin modern science and literature that in scholarly and industrial research organizations, today, there isenhanced interest in novel dosage forms that are maintained in the stomach for a prolonged andpredictableperiod.Regulating gastric residence time (GRT) is one of the most effective ways to promote continuous and predictable medication administration to the GI tract.i.e.dose form with gastro

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 UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, 2022

retention (GRDFs orGRDS) [4]. "Nutraceuticals" goods that are utilised for medical purposes in addition to being food. An ingredient with physiological benefits or that offers defence against chronic disease may be referred to as a nutraceutical product.Adietarysupplementisconsideredasaproductthat possesses or contains any of the following nutritional elements: A mineral, a vitamin, an amino acid, a medical herborotherbotanical,By increasing the total daily intake, the diet can be supplemented with a concentrate, metabolite, component, extract, or mixtures of these ingredients. Among these dietary supplements are nutraceuticals. which are used for health purposes other thannutrition. The types of gastro retentive dosage forms are: floating drug systems effervescent and non-effervescentsystems [5]. Hydrocolloids, polysaccharides, and polymer-forming matrix are commonly used in non-effervescent systems to generate polymers that take the form of gel or very swellable cellulose [6].

Effervescent systems use matrices made up of swellable polymers; for example, mythical R orchitosan, as well as effervescent substances like sodium bicarbonate, citric acid, or tartaric acid. [7]. There are numerous ways to ensure that dosage forms remain in the stomach, including floating, strong adhesion, swellable systems, hydrodynamically balanced systems, etc., sedimentation, expansion modifiedshape systems, and so on [8]. Floating drug delivery system (FDDS) has a lower volume density thangastricliquidsandthusstaysintheabdomenforalongtimewithout changing the rate of gastric emptyingThe gastric emptying rate gets prolonged when the FDDS system floats on the gastric contents, and thedrug is gradually released from the system at a required speed [9]. In order to create a customised release dosage forms, Xanthum gum was used as a matrix agent. Xanthum gum has been used to treatconstipation, diarrhoea, irritable bowel syndrome, inflammatory bowel illness, colitis ulcerative, coloncancer, diabetes, and hypercholesterolemia [10] Liquorice is made out of the dried, peeled or unpeeled roots and stolons of the Fabaceae family plant Glycyrrhiza glabra Linn [11]. It has been shown that liquorice works well to treat stomach ulcers.[12]andglycyrrhetinicacid.Aglyconeof glycyrrhizinhasanantiinflammatoryandantiulcerativeeffect[13].LiquoriceIt has also been claimed that liquorice extends the life of neurons on the stomach surface and has an anti-pepsin action. It has also been shown to raise prostaglandin concentration in the digestive tract, boosting stomach mucus secretion. Additionally, it has been found that licorice extract predisposes Helicobacter pylori to growth. [14].

2. MaterialsAnd Methods:-

2.1. Materials

The roots and rhizomes of Liquorice and Xanthan gum were purchased from the local market. Plantmaterials were authenticated by the Department of Pharmacognosy. The Herbarium specimen of theplantwasdepositedandidentifiedfromSamajshreePrashantdadaHirayCollegeofPharmacy,Malegaon. HPMC K100M was obtained from the Laboratory. Talc, Magnesium stearate. All chemicalsusedasreceivedwereofanalyticalandpharmaceuticalgrade.Theresearchuseddoubledistilledwat er.

ISSN PRINT 2319 1775 Online 2320 7876
 UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, 2022

2.2. Methods

2.2.1. ExtractionofLiquorice

The 250 milligrams of extract were refluxed in 50 mL of 1N HCl for 4 hours. Chloroform (20/5) mL was taken out once it had reached room temperature. In order to get rid of the chloroform extract, it was rinsed and filtered with water. At a temperature of 30 °C, the solution was evaporated. The residue was then dissolved in a mixture of one part chloroform to one part methanol, resulting in a volume of 25 ml.

2.2.2. FormulationofTablets

Inthisresearch,allthetabletswerepreparedusingDirect compression was used to create the tablets.usingpolymerHPMCK100MandothercomponentssuchasXanthangum,magnesiumstearate,talcandsodiumbicarbonate.All ingredients were accurately weighed after being correctly filtered using Sieve No. 80. The extract, HPMC K100 M, sodium bicarbonate, and Xanthan gum were successfully blended in a mortar and pestle to create a consistent tablet combination. Talc and magnesium stearate were finally incorporated into the mixture. The tablet mixture was then divided into different portions and crushed into tablets using a direct compression machine in accordance with the formula[15].

Table1.Compositionoffloatingtabletformulations.

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7
Xanthangum	125	100	75	100	100	100	100
Liquorice Extract	250	250	250	250	250	250	250
HPMCK100M	50	50	50	40	60	50	50
Sodium Bicarbonate	100	100	100	100	100	100	100
Talc	20	20	20	20	20	20	20
Magnesium Stearate	5	5	5	5	5	5	5

Directcompressionmethod

Direct Compression is the most straight forward manufacturing option , with the fewest manufacturingsteps , making it the easiest to control and least expensive . Excipients in API and compressing the completed tablets are the two main phases in the direct compression tablet process..Directcompressionisthemostadvancedtechnology.Itinvolvesonlyblendingandcompression.presenting a benefit, especially in terms of quick production. Due to the fact that it involves significantly fewer unit operations, less machinery, fewer employees, and less processing time along withincreasedproductstability .

ISSN PRINT 2319 1775 Online 2320 7876
 UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, 2022

RoleofDiluents

If the pill is unable to produce the desired volume, diluents are utilized as fillers to cover the discrepancy. Diluents used as disintegrants in dispersible and orally disintegrating tablets. For instance, calcium salts, lactose that has been spray-dried, starch, mannitol, sorbitol, and MCC

.RoleofBinders

Tablets contain binders as a binding agent because they provide powdered medications a cohesive strength..E.g.Gelatin , Glucose , Lactose , Cellulose derivatives , Methyl cellulose , Ethyl Cellulose , Hydroxypropylmethyl cellulose ,poly vinylpyrrolidone, starch,sodiumalginate ,Acacia ,etc.

RoleofLubricants

It is utilised to inhibit tablet adherence to dies and punches and minimise friction between die walls and tablets.E.g. Talc ,paraffin , stearicacid , sodiumbenzoate, etc.

3. Evaluation

3.1. PhysicalEvaluation

Physical Assessment Vernier callipers were used to measure and evaluate the thickness of the manufactured floating tablets. Using a Monsanto hardness analyzer, the tablets' hardness was evaluated. A Roche friabilator was used to determine the friability. Twenty tablets from each formulation were weighed and their averageweightwas determined andpresented in Table 2[16].

Table 2. Evaluationofformulatedtablets.

Formulation	Thickness (mm)	Diameter (mm)	Hardness (kg/cm)	Friability (%)	Uniformity of weight (mg)	Drug content (%)	Buoyancy time(Minute)
F1	4.02	11.166	3.133	0.85	510.4	97.273	5
F2	4.016	11.31	3.26	0.716	515.285	99.61	4
F3	4.04	11.73	3.23	0.804	530.16	97.44	5
F4	4.07	11.7	3.4	0.77	532.2	98.52	3.5
F5	4.04	11.4	3.36	0.81	52.2	96.10	5
F6	4.035	11.833	3.2	0.826	540.6	98.527	4
F7	4.046	11.543	3.1	0.868	520.3	98.02	4.5

ISSN PRINT 2319 1775 Online 2320 7876
Research paper UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, 2022

Fig.1.FloatingTablettime

Fig.2.FloatingTabletTimeAfter30min

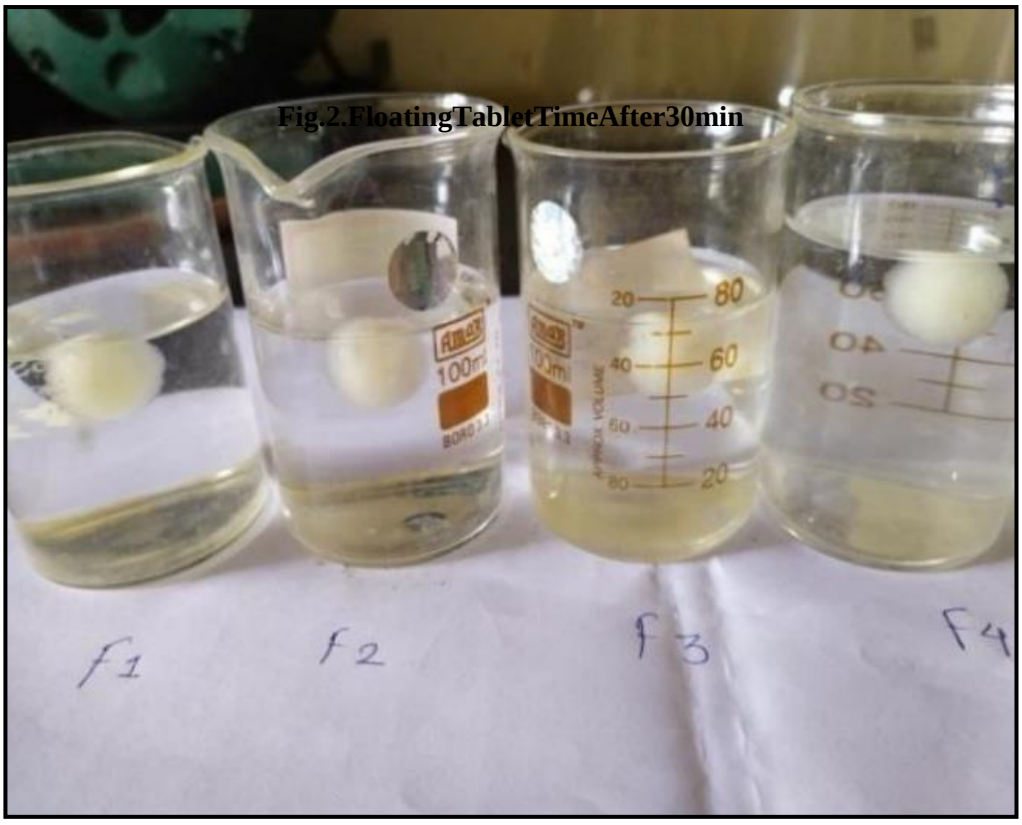


Fig.3.FloatingTablet TimeAfter40min

ISSN PRINT 2319 1775 Online 2320 7876
 UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, 2022

Fig.4. After2 hours

3.2. BuoyancyTime

Floating lag time (FLT) or buoyancy lag time (BLT) is the amount of time needed for a dosage form to surface on the medium. A USP class II (paddle) B apparatus was used to conduct floating behaviour investigations at a speed of 100 rpm in 900 mL of 0.1N HCl at a temperature of 37 0.2°C to simulate in vivo circumstances. On the basis of a visual inspection, FLT was determined.whichis shownin Fig.(1) andFig.(2)[17].

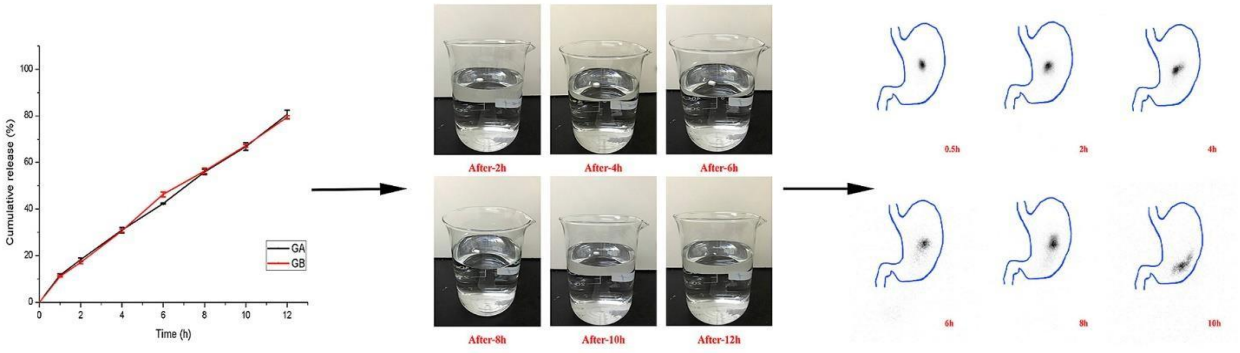
3.3. DrugReleaseIn-vitro

The in-vitro dissolution studies were carried out using USP type I (basket) apparatus. The dissolutionmediumwas900mL0.1NHCl.Thedissolutionmediumwaskeptinathermostaticallycontrolledwaterbath, maintained at 37±0.5°C. The tablet was placed into the basket and the speed of rotation was keptat 100 rpm The dissolution medium was kept constant throughout the procedure by replacing the 5 mL of sample at regular intervals with an equal amount of the dissolution medium. The aliquots were extracted using 30 mL of chloroform, and the chloroform fraction was tested for drug release using a spectrophotometric method at 251 nm in comparison to control chloroform. The investigation was carried out three times. [18].

3.4AnalysisofReleaseKinetics

The mechanism of release was determined by fitting the release data to the various kinetic equationssuch as firstorder, zero-order, Higuchi, and Korsmeyer-Pappas and the R2 values of the release profilecorrespondingtoeachmodelwere found.The resultsare shown inTable 3[19].

ISSN PRINT 2319 1775 Online 2320 7876
 UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, 2022



In vitro dissolution studies and release kinetics

In vitro floating behavior

In vivo buoyancy characterization

Fig.5.TabletFloatingto BuoyancyTest

4. Results

Alltheformulationswerepreparedsuccessfullybyusing Xanthumgumandliquoriceextract.

4.1. EvaluationofFormulatedTablets

All of the formulations had a diameter between 11.310 and 11.833 mm and a thickness between 4.0 and 4.071 mm. The hardness was in the 3.1–3.4 kg/cm range. (Table 2) [20].

4.2. BuoyancyTime

Boating Time Table 2 displays the formulas' buoyancy times. All formulations' FLT was found to be less than 5 minutes.. [21].

4.3DrugReleaseIn-vitro

Weperformedin-vitrodrugstudiesin0.1NHClasthedissolutionmedium.Theeffectoninvitroreleaseof Xanthum gum is presented in Fig. (1). As the xanthum gum concentration decreased from 125 (F1)to75mg(F3)pertablet,thepercentageofcumulativedrugreleaseincreasedfrom98,527±0.662%(F1)to 98,026±0.902% (F2). The cumulative drug release for (F3) after 8 hrs. was 97.273±0.499 percent,whichis shown in Figs. (3,4, and 5) [22].

4.4. AnalysisofReleaseKinetics

To study the release rate kinetics and the release mechanism of the drug from the tablet formulations,the in vitro drug release data were analysed by the mathematical equation such as first-order kineticsequation, zero-orderkineticsequation, Higuchi's equation, andKorsemeyer's equation.Thedataobtained are represented in Table 3. For all the formulations, the value of n was 0.6242-0.8408,suggesting an anomalous transport in which both diffusion and polymer relaxation

ISSN PRINT 2319 1775 Online 2320 7876
 UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, 2022

control the drugreleasemechanism[23].

Table 3.Analysisofrelease mechanism.

Formulation	Zeroorder R2	Firstorder R2	Firstorder kh-1	Higuchi R2	Korsmeyer R2	Korsmeyer n
F1	0.94	0.7658	0.3075	0.9908	0.9973	0.6141
F2	0.935	0.9275	0.2134	0.9865	0.9949	0.625
F3	0.9698	0.9261	0.2052	0.9714	0.9954	0.6177
F4	0.9812	0.9141	0.1651	0.9523	0.9982	0.7408
F5	0.9403	0.9061	0.2345	0.9799	0.9817	0.6295
F6	0.9568	0.9039	0.2015	0.9794	0.9973	0.6793
F7	0.9651	0.9119	0.1496	0.9738	0.9904	0.6688

4.5. OptimizationofTabletFormulation

The idealized formulation was discovered to be F7. The buoyant period lasted 3.5 minutes. and the percentagecumulativedrug release was 98.3% [24].

5. Discussion

5.1. EvaluationofFormulatedTablets

AlltheformulationspassedtheUSPrequirementsforfriabilityanduniformityofweight.

5.2. BuoyancyTime

Within the swelling polymer's gellified layer(hydrocolloids),thecarbondioxideproducedfromsodiumbicarbonateaftercontactwiththeacidicmediumwillstaytrapped.Thiscreatesandretainsitsbuoyancywithanupwardmotionofthedosageform.TheFLTisexplainedbythetimeittakesforthedissolutionmedium to penetrate the tablet matrix and to develop the swollen layer for in situ generated CO2trapping. Due to CO2 release and drug release from the matrix, the tablet mass reduced gradually. Ontheotherhand,theswellingoftheHPMCK100Mtriggeredanincreaseintabletquantityasthesolventpenetrated the glassy polymer layer. The combined impact is a net decrease in tablet density, whichextendsthefloatingtime beyond 8 hr. The combined effect results in a net reduction in tablet density, extending the floating time past 8 hours.

5.3. DrugReleaseIn-vitro

Drug Release In-vitro Xanthum gum gelling characteristics may have been attributed to the tablet's

ISSN PRINT 2319 1775 Online 2320 7876
 UGC CARE Listed (Group -I) Journal Volume 11, Iss 11, 2022

sluggish release. The effect onthe in-vitro release of various concentrations of HPMC K100 M is shown in Fig. (2). As the HPMCK100 M level increased from 40 (F4) to 60 mg (F5), the release of drugs declined from 99.61±0.631%to97.442±0.521%.Thismaybeduetotheenhancedconcentrationofpolymersthatshortensthe diffusionrouteforthedrug,whichmaydelaythereleaseofthedrug.Fig.(3)showstheimpactofsodiumbicarbonateonthein-vitrodrugrelease.Sodiumbicarbonatefunctionsasagas-generatingagentinsuchsystems. When it comes into contact with an acidic stomach environment, it produces gas. The water-soluble polymer matrix entraps the gas, and the formulation floats in the stomach's acidic environment. AnalysisofReleaseKinetics

WhenHiguchi'sequationwasusedtolearnthedrugreleasesystem,it wasnotedthatthevaluesdidnotprovide a good fit for the Higuchi equation. None of the formulations followed the kinetics of the firstorder,verifiedbytheinappropriatecorrelationcoefficientvalues.EquationsofKorsemeyerandPeppas(R^2 = 0.9817-0.9982) were best suited for all the formulations. When n is 0.5, it shows the controlledreleaseofdrugsbyFickiandiffusionandatthevalue1.0,itshowscaseIItransport(swelling-controlledrelease of drugs). Values of n between 0.5 and 1.0 are considered as a non-Fickian (anomaloustransportation)diffusionindicator.

5.4. OptimizationofTabletFormulation

Based upon the buoyancy time and percentage cumulative drug release, formulations were optimized.All of the formulations' buoyancy times fell between 3.5 and 5 minutes. The range of the cumulative total drug release was between 93.34 and 99.

6.Conclusion

The balance in floating and drug release profile has been accomplished. Formulation F7 has shownexcellentfloatingconductalongwithbetter-controlleddrugreleasecomparedtootherpreparedformulations.Therefore,boththediffusionandpolymerrelaxationcontrolthedrugreleasemechanism.We can conclude that sodium bicarbonate and HPMC K100 M in a mixture can act as a promisingpolymerforbuoyancy,helpfulforregulatingthedrugfloatingandalsothereleaseofdrugs.Thecurrentwork can, therefore, be regarded as a platform, providing information related to the development ofxanthum gumandliquoricefloating formulations.

7.Conflict of Interest: Authors have declared that no competing interests exist.

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ISSN PRINT 2319 1775 Online 2320 7876
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