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FLOATING *IN-SITU* RAFT FORMING LIQUID GASTRORETENTIVE DRUG DELIVERY SYSTEM CONTAINING POORLY WATER-SOLUBLE DRUG

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Present work was aimed to develop a liquid in-situ raft forming floating gastroretentive system of repaglinide using gellan gum, pectin, and sodium alginate. The formulations were characterized in terms of compatibility of drug-excipient by Fourier transform infrared, drug content, effect of processing parameters on physical form of drug (crystalline or amorphous) by X-ray diffraction analysis, thermal behaviour by differential scanning calorimetry, and in-vitro drug release study. The results confirm no interaction between the drug-excipients and fusion of drug crystals within the polymer matrix in amorphous form. The gel raft-floated for more than 24 hrs.. All the formulations showed instantaneous gelation within 30 seconds in 0.1 N HCl (pH 1.2). Formulation containing gellan gum (500 mg), pectin (500 mg), and glycerol monostearate (500 mg) released 21% of the drug in first 4 hrs., 69% in 6 hrs. and reached 97% in 7 hrs. Without gellan gum, 35% of the drug was released in the first 2 hrs. and reached 90% in 4 hrs. Based on these results it is suggested that the incorporation of drug into the liquid in-situ raft forming floating system may be an appropriate strategy to improve the dissolution profile of poorly soluble drugs.

INTRODUCTION

Oral route is the most convenient and preferred route for drug administration due to patient compliance. For maintaining drug concentration in the required therapeutic range, a conventional system needs to administer several times a day. This may cause considerable fluctuation in plasma drug concentration[1]. This has increased the demand for the development of controlled release drug delivery systems. An approximately planned controlled released drug delivery system can be a promising approach to overcome these two issues. The target of controlled release drug delivery incorporates two significant aspects namely spatial placement and temporal delivery of the drug. Spatial placement identifies with focusing on medication to a particular organ or tissue, while temporal conveyance alludes to controlling the rate of drug delivery to the target tissue[2]. However, a controlled release system may offer limited benefits for the drugs that have a narrow therapeutic window in the stomach or upper small intestine.

To increase the oral bioavailability of such drugs, the gastric residence time of formulation needs to be increased[3]. These systems may offer better alternative for the treatment of disease using existing drug molecules. Gastroretentive floating systems (GRFS) have been reported to overcome the bioavailability limitation of the drugs due to their poor absorption from the stomach or upper small intestine[4]. An optimum gastroretentive floating system is one which is retained in the stomach for prolonged time against all the physiological barriers like contractions, crushing, grinding, and peristaltic waves in the stomach, exhibit controlled drug release in acidic envirnment and finally metabolized[5-7]. Various techniques include floating *in-situ* raft forming drug dosage systems have been proposed to increase

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the gastric residence time[8]. The structure engaged with the raft formation recalls the arrangement of viscous cohesive gel and expands as a layer on the top of gastric fluid. This raft floats on gastric fluid because of the low mass thickness made by the course of action of carbon-di-oxide[9]. The system remains in the stomach without influencing gastric discharging rate for a deferred timeframe[10]. These systems are fluids or dispersions at room temperature undergo through gelation when interacted with body fluids containing particles or because of pH change. These frameworks show a unique property of either temperature-dependent or cation actuated gelation, which assurances maintained and site explicit medication conveyance[11]. The formed gels stay intact inside the stomach for a few hours bringing about prolonged or delayed medication conveyance in the upper part of gastrointestinal tract[12]. However, the success of these systems depends on the availability of sufficient fluid volume and acidic environment within the stomach[13].

Diabetes is a congregation of metabolic sickness characterized by hyperglycemia due to imperfections in insulin discharge, insulin activity, or both. The persistent hyperglycemia is related to long-duration harm, dysfunction, and collapse of different organs, particularly kidneys, heart, eyes, nerves, and veins. Rapid absorption of the drug and maintenance of dose for a prolonged time is the basic requirement to control blood glucose level in diabetic patients[14].

Repaglinide (2-ethoxy-4-[2-[[(1S)-3-methyl-1-(2-piperidin-1-ylphenyl) butyl] amino]-2-oxoethyl] benzoic acid) is an oral antihyperglycemic specialist utilized for the treatment of non-insulin-dependent diabetes mellitus (Figure 1). It belongs to the meglitinide class of short-acting insulin secretagogues, which act by binding to β cells of the pancreas to invigorate insulin discharge[15,16]. The elimination half-life of repaglinide is 1 hr. The mean absolute bioavailability is 56% when repaglinide is given with food. It has low water solubility (34 µg/mL at 37ºC) and high lipophilicity (log P= 3.97)[17].

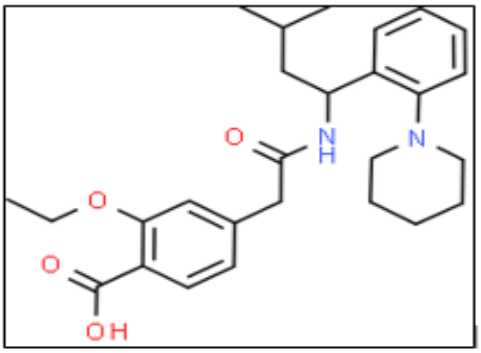

Fig. 1: Chemical structure of repaglinide

The purpose of this study is to explore liquid *in-situ* raft forming gastroretentive system for the controlled delivery of repaglinide. To achieve this objective, repaglinide containing liquid *in-situ* raft forming gastroretentive system was synthesized using sodium alginate, gellan gum, pectin, and glycerol monostearate. The effect of various polymer types and polymer concentration were examined. The synthesized liquid *in-situ* raft forming gastroretentive system was subsequently characterized for drug-excipient interaction study, X-ray diffraction study, thermal analysis, drug content, *in-vitro* gelling capacity, buoyancy, viscosity measurement, and *in-vitro* drug release profile.

MATERIAL AND METHODS

Materials

Repaglinide was received as a gift sample from Dr. Reddy's Laboratories, Hyderabad, India. Gellan gum was purchased from Sisco Research Laboratories Pvt. Ltd., Maharashtra, India. Pectin (DE 28-45%) was purchased from Krishna Pectins Pvt. Ltd., Maharashtra, India. Sodium alginate and glycerol monostearate (GMS) were purchased from Central Drug House (P) Ltd., New Delhi, India. Sodium methylparaben was purchased from Arora & Co., Delhi, India. Calcium carbonate was purchased from Sisco Research Laboratories Pvt. Ltd., Maharashtra, India. Sodium citrate was purchased from Thermo Electron LLS India Pvt. Ltd., Mumbai, India.

Preparation of repaglinide GRFS

Sodium alginate (a chelating agent) was dispersed in deionized water under stirring. In another beaker, gellan gum was added to

deionized water containing sodium citrate. Both the solutions were mixed using a magnetic stirrer (REMI Elektrotechnik Limited, Mumbai, India) and GMS was added. The temperature was maintained at 90°C. After cooling to 40°C, pectin solution containing calcium carbonate and repaglinide was added with consistent stirring till the homogenous thick polymeric solution was obtained. Sodium methylparaben was added to the homogenous thick drug containing polymeric solution (Table 1). The formulation was degassed using a sonicator (Life Care Equipments Private Limited, Mumbai, India)[18-20].

Determination of drug content

Drug content was determined by dissolving ten milliliters of formulation in 50 mL of methanol. The mixture was kept aside for 24 hrs. with intermittent stirring using a magnetic stirrer for complete extraction of drug from the polymeric system. After 24 hrs., the mixture was filtered through Whatman filter paper. The filtrate was analyzed spectrophotometrically at 244 nm using a UV spectrophotometer (3200, Labindia, Mumbai, India) to estimate the content of repaglinide in the sample[21].

Determination of *in-vitro* buoyancy

The floating behaviour was recorded by introducing 2 mL of the GRFS into 100 mL of 0.1 N HCl (pH 1.2) in a 100 mL measuring cylinder. The time taken by the formulation to come back to the surface of the medium was recorded as buoyancy lag time (BLT). The time till which the formulation remained on the surface of the medium was recorded as total floating time[11&18&20&22].

Determination of *in-vitro* gelling capacity

Two milliliters of the formulation was carefully positioned into a measuring cylinder. Six milliliters of 0.1 N HCl (pH 1.2) was added gradually, and the gelation was accessed visually. The gelling capacity was scored in three categories (gels after couple of moments and dispersed rapidly, quick gelation and remains for 12 hrs., and quick gelation and remains for more than 12 hrs.) dependent on gelation time and period for which formed gel remained[18&19&22].

Drug-excipient interaction study

A drug-excipient interaction study was carried out using a Fourier transform infrared (FTIR) spectrophotometer (IR affinity-1, Shimadzu, Japan)[23]. The FTIR spectral data of repaglinide and formulation F1 were taken for the determination of potential molecular interactions between the drug and excipients. The samples were gently triturated with KBr powder and compacted into a disc using a KBr press at 10 tons. The sample scanning was carried out from 4000 to 400 cm^{-1} at a resolution of 4 cm^{-1}.

Table 1: Composition of liquid *in-situ* raft forming gastroretentiv system (for 100 mL)

Ingredients (mg)	Formulation code								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Repaglinide	250	250	250	250	250	250	250	250	250
Gellan gum	500	0	250	500	1000	500	0	1000	750
Pectin	500	250	250	500	750	750	0	1000	1000
Sodium alginate	1500	1500	1500	1500	1500	1500	1500	1500	1500
GMS	500	250	250	1000	750	750	0	1000	1000
Sodium methyl paraben	200	200	200	200	200	200	200	200	200
Calcium carbonate	250	250	250	250	250	250	250	250	250
Sodium citrate	250	250	250	250	250	250	250	250	250

X-ray diffraction study

To analyze the physical form of the drug in the optimized formula, the X-ray diffractograms of pure repaglinide and formulation F1 were recorded by X-ray powder diffractometer (PW 3040/60 Xpert PRO, Panlytical, Netherlands). The X-ray diffraction patterns were recorded using Cu Kα radiations (λ = 1.5405980 Å), a voltage of 40 kV, and a current of 30 mA. The samples were analyzed over 5-90 2θ range with a scan step size of 0.02 and 0.50 s/step[5].

Thermal analysis

Thermograms of pure repaglinide, sodium alginate, gellan gum, pectin, and formulation F1 were produced by differential scanning calorimeter (DSC Q20 V24.11 Build 124 instrument equipped with Universal V4.5A TA Instruments software). Zinc (419.5ºC), tin (232ºC), and indium (156ºC) were used as internal standards to calibrate the instrument. Accurately weighed samples were placed into a 40 mL aluminum pan. The probes were heated upto 400ºC at a rate of 10 K/min under nitrogen atmosphere[23].

Viscosity measurement

Viscosity measurements of formulation F1 (liquid and raft) were carried out using a Brookfield R/S Plus Rheometer (cone and plate model). The measuring system used was C-25 Din. The study was carried out at an angular velocity of 10, 20, 30, 40, 50, and 60 rpm and corresponding readings were recorded. Brookfield Rheo-2000 V2.8 software was used for the measurement of the rheological behaviour[24,25].

***In-vitro* drug release study**

Repaglinide release from the liquid floating raft formulations (formulation F1, F2, and F3) was determined using a USP dissolution test apparatus (type II) (TDT06L, Electrolab, Mumbai, India) at 50 rpm in 900 mL of 0.1N HCl (pH 1.2). The temperature of dissolution fluid was maintained at 37°C ± 0.5°C. A measured amount of the formulation equivalent to 50 mg repaglinide was added carefully to the dissolution vessel using a disposable syringe. The samples were (5 mL) withdrawn at each 30 min interval till 7 hrs. The sink condition was maintained by adding 5 mL of fresh dissolution fluid (maintained at the same temperature) after each withdrawal. The samples were filtered through a Whatman filter paper and analyzed using a UV spectrophotometer (3200, LabIndia, Mumbai, India). The sample analysis was carried in triplicate[18&19&22]. A graph of percentage cumulative drug released against time was plotted to access the dissolution profile of repaglinide from the developed floating raft formulations.

The *in-vitro* drug release data was statistically analyzed by two-way analysis of variance (ANOVA) followed by Tukey test using Graph Pad software (La Jolla, CA). The p value of < 0.0001 was considered statistically significant.

RESULTS AND DISCUSSION

Drug Content

Drug content was determined by UV spectrophotometric method. Drug content was found to be between 87.93 ± 0.58% and 97.15 ± 0.66% (Table 2). The maximum percentage of drug content *i.e.* 97.15 ± 0.66% is observed in case of formulation F1. The difference in the drug content among different formulations could be due to the difference in formulation viscosity associated with the polymer type and concentration used.

***In-vitro* buoyancy**

In presence of gastric fluid, calcium carbonate delivered calcium ion and carbon dioxide gas. The calcium ion interacted with alginate and gellan gum to form gel like consistency. Once the liquid formulation added to 0.1N HCl (pH 1.2), initially it sank to the bottom of the medium. At that point, the carbon-di-oxide was generated, and the gel moved up and was kept buoyant on the surface of the medium due to the entrapment of carbon dioxide within the gel network (Figure 2). The time that the formulation took to move from the bottom of the medium to its surface (buoyancy lag time) and the time that the formulation persisted on the medium surface (duration of floating) were recorded. The gel raft-maintained floating for more than 24 h, except formulation F2 and F7. Formulation F2 was buoyant for about 12 hrs., which could be due to the low viscosity of the formulation at low

polymer concentration. Formulation F7 did not contained pectin, gellan gum, and GMS, and the formed gel got dissolved quickly. Due to this, the entrapped carbon-di-oxide released quickly, and the formulation sank to the bottom after 6 h (Table 2). From experimental trials, it was observed that the formulation containing calcium carbonate had better floating ability than the formulation containing sodium carbonate (data not shown). The concentration of gellan gum, pectin and calcium carbonate influenced floating lag time. Floating lag time was reduced with an increase in calcium carbonate concentration. The increased concentration of gellan gum and pectin increased floating lag time and decreased floating duration.

Fig. 2: Results of *in-vitro* buoyancy study.

In- vitro gelling capacity

All the formulations showed rapid gelation (within 30 sec) in 0.1N HCl (pH 1.2) (Table 2 and Figure 3). Formulations without gellan gum with low level or without pectin showed quick gelation, but dissolves within 8 h. In case of formulation containing gellan gum and pectin at lower level showed quick gelation that was remained for > 12 hrs. GMS also had a significant role in gelling of the formulation. Formulations containing GMS at moderate of high concentration showed good gelling property for more than 24 hrs. Formulation containing calcium carbonate gelled more instantaneously than the formulation containing sodium carbonate (data not shown). Calcium carbonate present in the formulation as insoluble dispersion becomes soluble in an acidic medium and releases calcium ions leading to the gelation of formulation. Further, the divalent ions (Ca^{++}) can make a stronger gel than that of monovalent ions (Na^{+}). Additionally, at a higher concentration of calcium carbonate a stronger gel was formed whereas a weak gel was formed at a low concentration of calcium carbonate[20]. The high polymer concentration and calcium carbonate mixture resulted in an adequate gel strength when pressed with a pair of forceps, indicating that the gel can withstand the peristaltic movement in the stomach. Thus, the developed system is expected to have a longer residence time than that of oral solutions of repaglinide.

Table 2: Results of drug content, gelation, buoyancy lag time, and floating time of repaglinide containing GRFS.

Formulation code	Drug content (%)	Gelation (pH 1.2)	Buoyancy lag time (sec)	Floating time (h)
F1	97.15±0.66	+++	37	>24
F2	96.55±1.40	+	13	>12
F3	96.12±1.21	++	20	>24
F4	89.33±1.54	+++	63	>24
F5	89.37±1.04	+++	91	>24
F6	88.51±2.51	+++	69	>24
F7	88.22±0.39	+	3	> 6
F8	89.47±0.72	+++	105	>24
F9	87.93±0.58	+++	89	>24

+ quick gelation but dissolves within 8 h, ++ quick gelation and remained for > 12 h, +++ quick gelation and remained for > 20 h

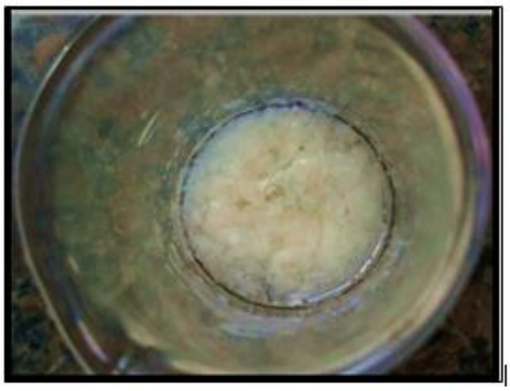

Fig. 3: Gel formation of GRFS in presence of 0.1N HCl (pH 1.2).

Drug-excipient interaction study

To check the compatibility of the drug with different excipients, the FTIR spectra of pure drugs and blend of the drug and excipients were taken (Figure 4). The FTIR spectrum of repaglinide revealed presence of N-H stretching vibration at 3306.73 cm^{-1}, carbonyl group (1606.59, 1634.56, and 1686.63 cm^{-1}, C-H stretching (2934.0 cm^{-1}), N-H bending (1634.56 cm^{-1}), aromatic ring (1566.02 cm^{-1}), 1428.19-1499.91 cm^{-1} (C-O stretching), CN stretching at 1040.52, 1090.67, 1148.53, and 1176.50 cm^{-1}, CH bending at 1449.41 cm^{-1} and CH stretching at 2852.52, 2866.02, 2920.03, 2934.49, 2965.35, and 2985.60 cm^{-1}. The spectrum portrayed by intense bands at 3300-2500 cm^{-1} due to the O-H stretching vibration. The characteristic peaks of the drug were also present in the spectrum of optimized formulation. However, some of the drug peaks were slightly shifted or the intensity decreased slightly. These results suggested that there was no interaction between the pure repaglinide and excipients.

X-ray diffraction studies

The powder X-ray diffraction pattern of the repaglinide and optimized formulation (formulation F1) are illustrated in Figure 5. Pure repaglinide showed various characteristic intense peaks at 2-theta (deg) of 7.6671, 10.1308, 12.4531, 13.8098, 14.637, 15.33, 16.6879, 17.5291, 18.6227, 20.4963, 22.5773, 22.9163, 23.9246, 26.1468, and 30.8285 indicating its crystalline nature. The developed GRFS did not show many of the characteristic intense peaks of repaglinide, indicating that the repaglinide in the developed GRFS converted in amorphous form

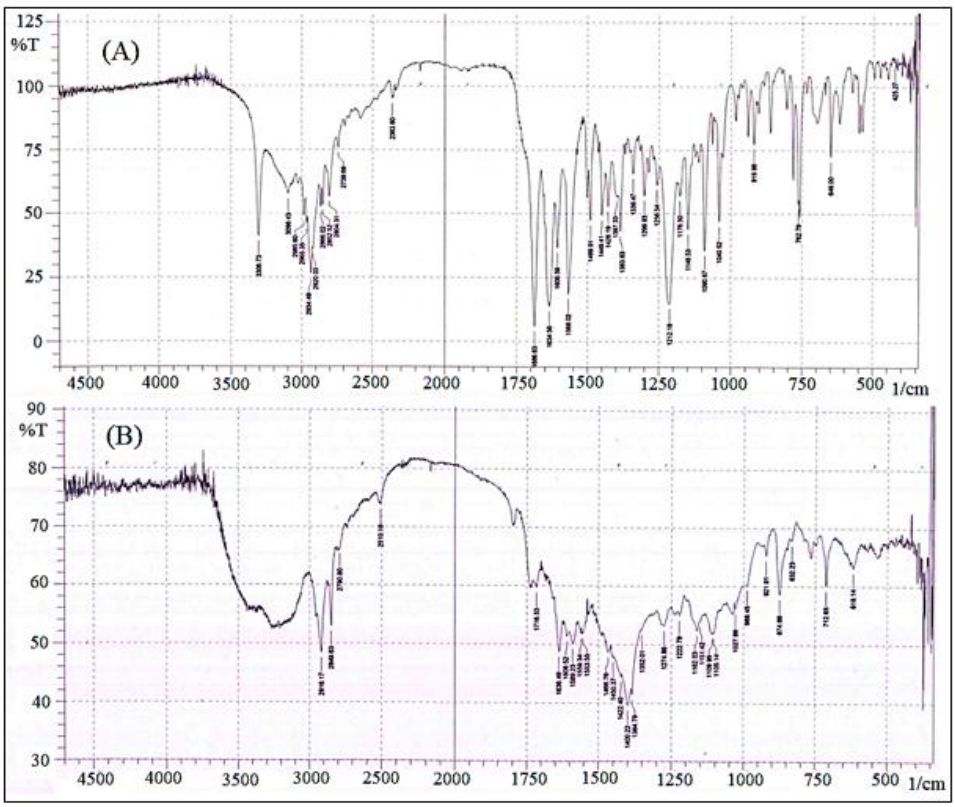

Fig. 4: FTIR of repaglinide (A) and optimized formulation (formulation F1).

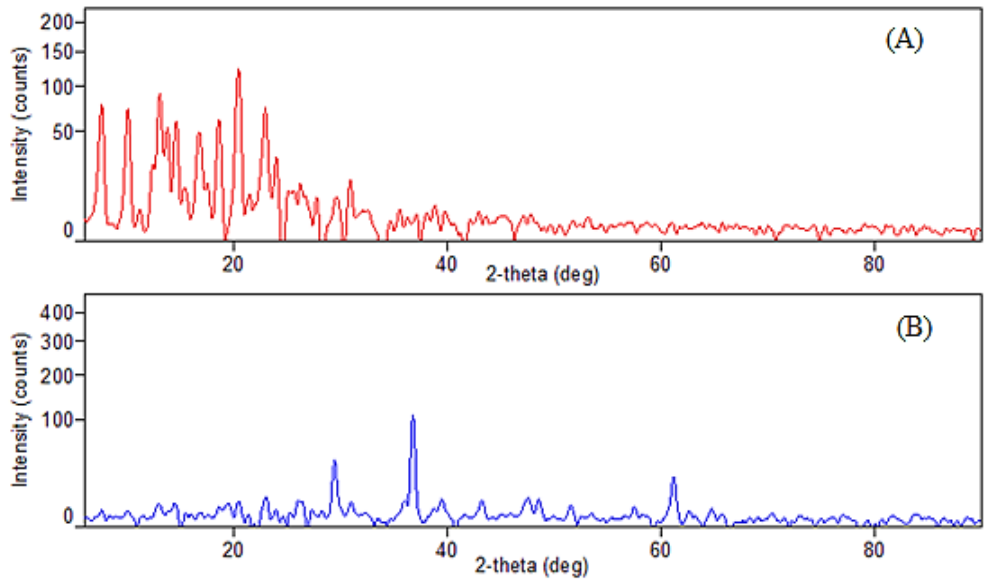

Fig. 5: X-ray diffractograms of pure repaglinide (A) and formulation F1 (B).

Thermal analysis

DSC thermograms of pure repaglinide, sodium alginate, gellan gum, pectin, and formulation F1 are shown in Figure 6. DSC thermogram of pure repaglinide showed an endothermic peak at 134.26ºC which was consistent with its melting point. The DSC thermogram of gellan gum exhibited an endothermic peak near 70°C and an exothermic peak at 260.41°C due to loss of absorbed moisture in sample and polymer degradation, respectively[26]. The endotherm at 188.7°C in the thermogram of pectin is due to the thermal degradation of pectin. Sodium alginate showed a broad endotherm and exotherm at 84.0°C due to the loss of moisture. The second exothermic peak at 259.2°C is due to the loss of volatile components, chain rupture, and fragmentation of sodium alginate[17]. The intensity of endothermic peak of repaglinide the DSC thermograms of repaglinide formulation containing soluble polymer was reduced (134.04ºC) as compared to the pure repaglinide indicating reduce crystallinity of repaglinide and its stabilization in amorphous structure. The reduced intensity of endothermic peak of drug also might be due to dilution effect of different excipients[27]. These results agree with the results of XRD study (Figure 5).

Viscosity Study

Viscosity is the most important parameter which needs to evaluate for a liquid floating raft forming system that plays an important role in controlling drug release and gastric retention of the formulation. Viscosity results of the formulation F1 (before and after raft formation) are shown in Figure 7. Pectin is recognized as viscosity enhancing agents and approved by US Food and Drug Administration (FDA) and is official in United States Pharmacopoeia (USP). Gellan gum (an excellent gelling polymer) is a natural polysaccharide derived from *Pseudomonas elodea*, composed of glucuronic acid, rhamnose and glucose, and O-acetyl moieties[28]. These polymers significantly imparted viscosity in the formulations. The viscosity of liquid formulation increased drastically when it formed raft in presence of 0.1 N HCl (pH 1.2). High viscosity can retard the escape of generated carbon-di-oxide within the polymer metrices and prolonged buoyancy duration. Higher viscosity values can also retard the drug release rate from formulation.

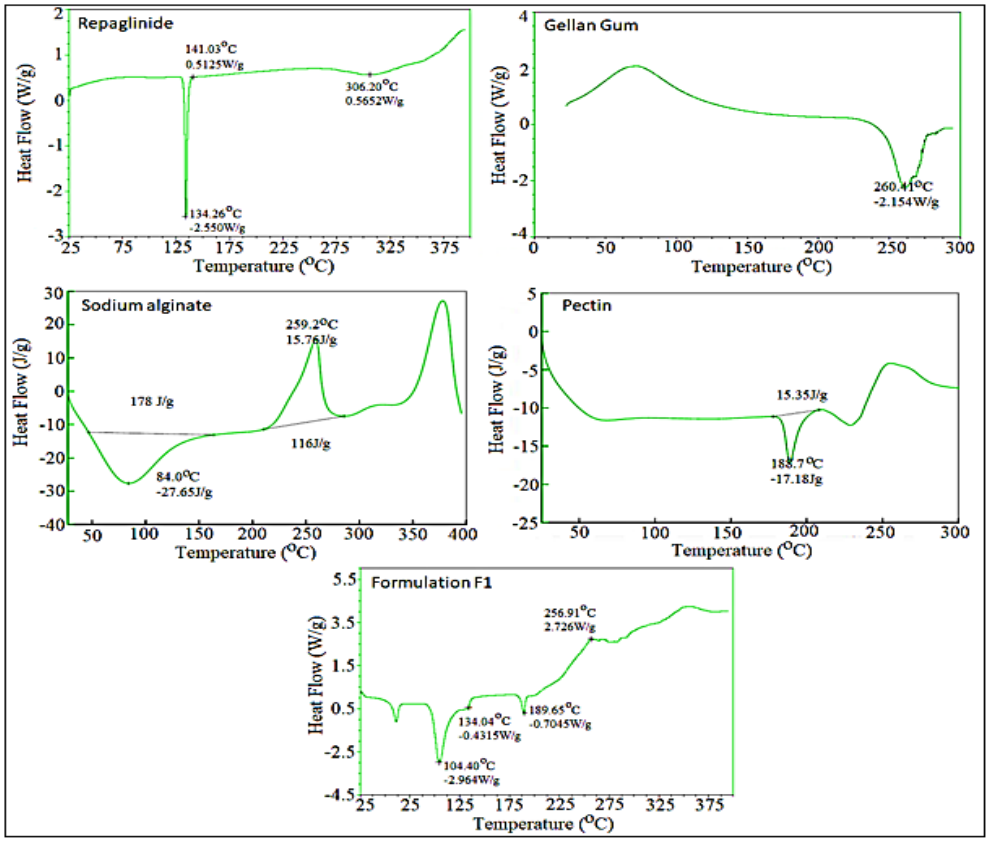

Fig. 6: DSC thermograms of pure repaglinide, sodium alginate, gellan gum, pectin, and formulation F1

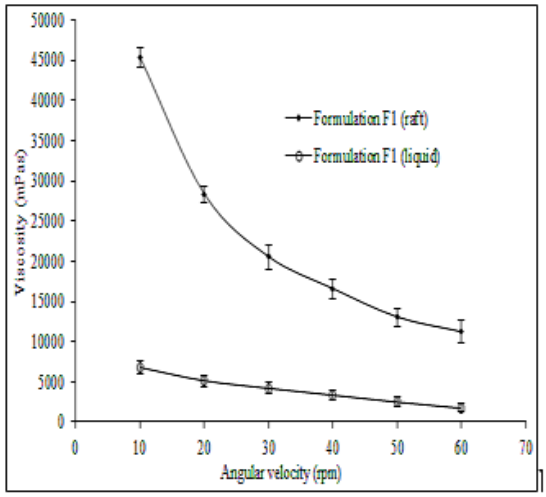

Fig. 7: Viscosity result of formulation F1 (liquid) and formulation F1 (raft) at 10, 20, 30, 40, 50, and 60 rpm (mean ± SD, n= 3).

In- vitro drug release studies

Figure 8 indicates a two-stage repaglinide release profile from the GRFS. The first phase was observed by a slow drug release profile. The second phase was characterized by a rapid drug release profile. From the formulation F_1 (containing gellan gum (500 mg), pectin (500 mg), and GMS (500 mg)) less than 10% repaglinide was released within 2 hrs., 21% of the drug in first 4 hrs., 69% in 6 hrs., and reached 97% in 7 hrs.. In the case of formulation F2, where gellan gum was not present, the drug release was 35% in the first 2 hrs. and reached 90% in 4 hrs. In formulation F3, where the concentration of gellan gum, pectin and GMS is half than that of formulation F1 *i.e.*, 250 mg each of gellan gum, pectin and GMS, the drug released was 14% in the first 2 hrs., 31% in 4 hrs. and 91% in 6 hrs. Sodium citrate complexes the free Ca^{2+} ions and only releases them in the acidic environment of the stomach. The cross-linking of polymer network and its gelation due to the Ca^{2+} ions occurred in acidic environment[18&19&29]. These results suggested that the sodium citrate and polymers had a significant effect on drug release profile.

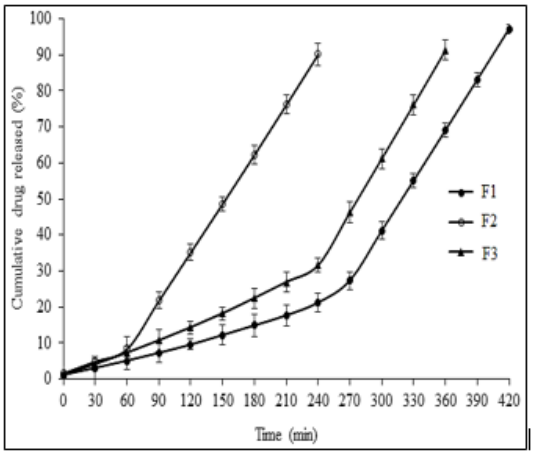

Fig. 8: *In-vitro* drug release profiles of formulation F1, F2, F3 of liquid GRFS containing repaglinide (filled circles F1, empty circles F2, and filled triangles F3) in 0.1N HCl (pH 1.2) at 37°C (mean ± SD, n=3).

The release data of repaglinide from GRFS was analysed using the zero order (Cumulative amount of percentage drug released against time) and first order (log percentage cumulative drug remaining against time) plots. Confirmation of the order of release was carried out using Higuchi's model (a plot of the cumulative percentage of drug released versus square root of time). To determine drug release mechanism and to verify the fact that whether diffusion is non-Fickian or Fickian, the slope (n) values were analysed according to Peppas' model (log cumulative percentage of drug release was plotted against log time). The n value less than or equal to 0.5 indicates diffusion controlled drug release without swelling. The n value between 0.5 and 1 indicates the drug release through diffusion with swelling. If the n value is more than 1, it indicates anomalous diffusion (non-Fickian). The linearity of the plots was confirmed by the calculation of correlation coefficient (r^2)[14]. The best fitting of models was based on goodness of fit *i.e.* the highest r^2. The results confirmed that the repaglinide dissolution from GRFS followed zero order kinetcs (Table 3). The Higuchi's plots showed linearity with correlation coefficient (r^2) values between 0.8653 and 0.9907. The diffusion mechanism of drug release was further confirmed by Peppas' plots that showed linearity for repaglinide release from GRFS (r^2 values between 0.9196 and 0.9898 with slope (n) values between 0.1113 and 0.1806), indicating diffusion-controlled drug release from the GRFS without swelling (Table 3).

On application of two-way ANOVA, the calculated F value was higher than the tabulated value indicating a significant difference in the *in-vitro* release profiles among formulation F1, F2, and F3 at 95% confidence interval ($p< 0.001$). This substantiates the role of polymers and sodium citrate in controlling drug release from GRFS (Table 4).

Table 3 : Results of kinetic study of repaglinide release from GRFS in 0.1N HCl (pH 1.2)

Formulation code	Model				
	Zero order	First order	Higuchi's model	Peppas' model	
	r^2	r^2	r^2	r^2	n
Formulation F1	0.8558	0.5793	0.8653	0.9898	0.1113
Formulation F2	0.9784	0.8469	0.9907	0.9196	0.1806
Formulation F3	0.8906	0.6827	0.8944	0.9811	0.1148

r^2 is correlation coefficient, n is the slope

Table 4. Results of ANOVA on the release profiles of repaglinide from GRFS in 0.1N HCl (pH 1.2)

Source of variation	Sum of square	Degree of freedom	Mean squares	Calculated F (DFn, DFd)	P value
Raw sum of squares	86860	14	6204	F (14, 93) = 48.31	P < 0.0001
Column sum of squares	13537	2	6768	F (2, 93) = 52.70	P < 0.0001
Error sum of squares	11944	93	128.4		

Conclusion

A liquid *in-situ* raft forming floating system for repaglinide was successfully developed. This liquid formulation can be easily gulped and quickly changed to a floating gel raft in the stomach. This liquid system is expected to provide clinicians with a safe choice of product for better control of blood sugar level. The formulation showed excellent buoyancy coupled with extended drug release from a hydrophilic matrix. The type and amount of polymer played the main role in *in-vitro* performance of the formulation. Buoyancy lag time increased with an increase in polymer concentration. Best drug release profile was obtained from formulation containing gellan gum (500 mg), and pectin (500 mg) in combination in presence of GMS (500 mg). The developed liquid floating formulation showed promising results in the preliminary laboratory tests. However, scale up studies and biopharmaceutical characterization are needed to establish these formulations.

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تكون نظام سائل ممد بالدواء طاف على سطح المحتوى المعوى يحتوى على عقار شحيح الذوبان فى الماء

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تم فى هذا البحث تطوير نظام داخلى طاف عل سطح المحتوى المعوى لعقار الريباجلينيد باستخدام صمغ الجيلان والبكتين وألجينات الصوديوم وتم دراسة التوافق الفيزيائى لجميع الصيغات المحضرة بواسطة الأشعة تحت الحمراء وكذلك حساب محتوى العقار كما تم دراسة تأثير طريقة التحضير على حالة العقار بواسطة حيود الأشعة السينية والماسح الحرارى التفاضلى وكذلك إنطلاق العقار من الصياغات المحضرة معمليا

وأثبتت النتائج أنه يوجد توافق تام بين العقار والصواغات المستعملة فى التحضير وقد تم تحول العقار من صورة بلورات إلى صورة مائعة وأن النظام الدوائى المحضر أستمر طافيا على سطح المحتوى المعدى لمدة ٢٤ ساعة وأن درجة تكون الجل كانت أقل من ٣٠ ثانية فى الوسط الحامضى

وكانت نسبة إنطلاق الدواء من الصياغة التى تحتوى على (٥٠٠ من كلا من البكتين وصمغ الجيلان وجليسرين أحادى الإستياريت) حوالى ٢١% بعد ٤ ساعات و ٦٩ % بعد ٦ ساعات و ٩٧ % بعد ٧ ساعات بينما كان إنطلاق الدواء ٣٥ % فى أول ساعتين ووصل إلى ٩٠ % بعد ٤ ساعات فى الصياغة التى لا تحتوى على صمغ الجيلان

وبناء على النتائج السابقة توصلت الدراسة إلى إنه بتحضير سائل يتحول إلى جيل على سطح المحتوى المعوى كنظام ممد بالدواء يمكن زيادة الذائبية للعقارات شحيحة الذوبان فى الماء