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Original Article

FLOATING-BIOADHESIVE MATRIX TABLETS OF HYDRALAZINE HCL MADE OF CASHEW GUM AND HPMC K4M

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ABSTRACT

Objective: The objective of this paper was to prepare and evaluate floating-bioadhesive cashew gum-hydroxypropyl methylcellulose (HPMC K4M) matrix tablets for the gastro-retentive release of hydralazine HCl.

Methods: The cashew gum-HPMC K4M matrix tablets of hydralazine HCl were prepared by direct compression method with the incorporation of sodium bicarbonate and citric acid as effervescent agents. Drug contents, weight variations, hardness, friability, *in vitro* swelling, *in vitro* floatation, *ex vivo* mucoadhesion and *in vitro* drug release of these matrix tablets were evaluated.

Results: Drug contents, weight variations, hardness and friability of these matrix tablets were within the compendia limits. These tablets were floated well *in vitro* over 12 h in simulated gastric fluid (SGF, pH 1.2) with minimum lag time. The *ex vivo* adhesion of these matrix tablets with goat intestinal mucosa exhibited good bioadhesion in a wash off test. All these cashew gum-HPMC K4M floating-bioadhesive matrix tablets of hydralazine HCl showed *in vitro* sustained releases of hydralazine HCl over 12 h in SGF, pH 1.2. The *in vitro* hydralazine HCl followed Korsmeyer-Peppas kinetic model and anomalous (non-Fickian) diffusion mechanism. The drug-polymer compatibility analysis by FTIR spectroscopy indicated the absence of any drug-polymer interaction within this cashew gum-HPMC K4M floating-bioadhesive matrix tablets of hydralazine HCl.

Conclusion: The results clearly indicate a promising potential of the use of cashew gum as matrix forming a material with HPMC K4M to prepare matrix tablets for gastro retentive delivery of hydralazine HCl through the combined approach of floatation and bioadhesion to reduce the dosing rate with better patient compliances.

Keywords: Cashew gum, HPMC K4M, Flotation, Bioadhesion, Hydralazine HCl

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INTRODUCTION

Now a day, a variety of drug delivery devices has been explored to retain in the gastrointestinal tract (GIT) [1-3]. In both academia and industry, a lot of efforts have been made towards the development of numerous types of gastro retentive deliveries for several drug candidates [4-5]. Floating dosage forms as compared to other gastroretentive techniques are very popular technology to achieve the most effective and coherent protection against early and random times of gastric emptying [6-10]. One of the most important and widely used techniques for the development of these floating drug delivery systems is to use low-density materials [11-14]. Beside this, to achieve the float ability, an effervescent technique based gastro retentive floating dosage forms are being designed to be remained buoyant on the gastric fluid using carbon dioxide gas (CO_2) generating agents (*e. g.,* sodium bicarbonate, citric acid or tartaric acid) [15-17]. CO_2 is liberated in the GIT after oral administration from these drug delivery systems and this make it to float on the gastric fluid because it reduces the density of the system and thus, retained in the stomach for several hours [18]. As a result of this, the drug is slowly released at a desired rate which results in an enhanced gastric retention time as well as a better control of the fluctuation in plasma drug concentration and thus, increases the bioavailability. Currently, floatation and bioadhesion approaches are being extensively examined to improve therapeutic efficacy by maximizing bioavailability through gastro retention of the dosage form [19-29]. Recent years, the combination of floatation and bioadhesion approaches has gained importance in the development of gastro retentive drug delivery system [30-33]. In this study, attempts were made to formulate gastroretentive floating-bioadhesive drug delivery systems using blends of a plant-derived natural gum, cashew gum and a semi-synthetic gum, HPMC K4M.

Cashew gum is a plant-derived natural gum, extracted from the incised trunk of the tree, *Anacardium occidentale* (belonging to the family: Anacardiaceae) [34]. It is a complex polysaccharidic gum comprising glucose, arabinose, galactose, rhamnose, mannose, glucuronic acid and other sugar residues [35]. Cashew gum is biodegradable and biocompatible [36]. Recent years, cashew gum has been widely studied for pharmaceutical, cosmeceutical and food applications [34, 36-38]. It is studied as a binding agent and matrix-forming agent in the formulation of various pharmaceutical tablets [34, 36, 39-40]. Cashew gum was also investigated as matrix-forming material in the formulation of floating systems [41]. Therefore on the basis of results of these investigations, the formulation of a new gastroretentive matrix system (made of cashew gum and HPMC K4M) comprising a combination of floatation and bioadhesion approaches was planned to control sustained release of hydralazine HCl.

Hydralazine is a directly acting vasodilator and widely prescribed in the treatment of hypertension and congestive heart failure [42]. Following oral administration, it is readily absorbed and subjected to significant first-pass metabolism [42-43]. It is reported for a short biological half-life of 2–4 h [43-44]. Therefore, to produce better patient compliance by reducing the dosing frequencies and enhanced oral bioavailability sustained release gastro retentive dosage forms of hydralazine might be beneficial. In the literature, no research is reported for the preparation of floating-bioadhesive matrix tablets made of cashew gum-HPMC K4M blends. The main goal of this study was the preparation and evaluation of floating-bioadhesive cashew gum-HPMC K4M matrix tablets for gastro retentive release of hydralazine HCl.

MATERIALS AND METHODS

Materials

Hydralazine HCl was a gift from Hetero Drugs Ltd., India. HPMC K4M (Matrix Laboratories, India), lactose (Reidel India Chemicals, India), sodium carbonate (B. D. Pharmaceutical, India), citric acid (Loba Chemie Pvt. Ltd., India), magnesium stearate (Loba Chemie Pvt. Ltd.,

India), talc (Nice Chemie Pvt. Ltd., India) were used. Cashew gum was extracted from crude cashew tree exudate, which was collected at Jharpokharia, Odisha, India in the month of September 2015. All the other chemicals and reagents used were of analytical grade and commercially available.

Extraction of cashew gum

The crude cashew tree exudate was cleaned by removing bark pieces and further extraneous substances. The crude exudate was dried in a tray drier at 50±2 °C for 10 h until it became brittle. The dried exudate were reduced to powder through milling in a domestic blender and then, sieving. 1 kg of the crude cashew tree exudate powder was dissolved in 2 liter distilled water and the exudate solution was boiled for 1 hour under occasional stirring in a temperature controlled water bath. After cooling at room temperature, the resulting exudate solution was further cooled by keeping in a refrigerator overnight to settle out proteins and undissolved materials, if occurred. The upper solution was decanted and then, concentrated at 50±2 °C by a temperature controlled water bath to 1/3rd of its original volume. After cooling the concentrated cashew tree exudate solution at room temperature, it was poured into twice the volume of acetone with continuous stirring. The formed precipitate was filtered and washed repeatedly with acetone. The collected precipitate was dried in a tray drier at 50±2 °C for 10 h. The obtained dried film of precipitate was milled to fine powder of cashew gum and sieved through sieve number 80. The extracted cashew gum was kept in an air-tight desiccator until further use [37].

Preparation of matrix tablets containing hydralazine HCl

By direct compression method, the floating-bioadhesive matrix tablets of hydralazine HCl were prepared after proper mixing of suitable ratios of various excipients. Except glidant and lubricant, all the ingredients were thoroughly mixed and passed through sieve # 80. After that, all the excipients along with hydralazine HCl (50 mg) were uniformly mixed and compressed by a single punch tablet machine (Cadmach Machinery Co. Pvt. Ltd., India) utilizing 9 mm round and concave punches (for a batch size of 50 tablets). The compositions of hydralazine HCl floating bioadhesive matrix tablets are presented in table 1.

Table 1: Compositions of cashew gum-HPMC K4M floating-bioadhesive matrix tablets containing hydralazine HCl

Ingredients*	Formulation codes			
	F1	F2	F3	F4
Drug	50	50	50	50
HPMC K 4M[a]	50	50	50	50
Cashew gum	-	50	75	100
$NaHCO_3$	35	35	35	35
Citric acid	10	10	10	10
Magnesium stearate	5	5	5	5
Talc	5	5	5	5
MCC PH 102[b]	20	20	20	20
Lactose	110	60	35	10
Total weight	300	300	300	300

*All values mentioned above are in mg, [a]HPMC K4M = hydroxypropyl methylcellulose (K4M), [b]MCC PH 102 = Microcrystalline cellulose (PH 102)

Determination of hydralazine HCl

For simultaneous determination of hydralazine HCl, an UV-VIS Spectrophotometer (SHIMADZU, Japan) with matched quartz cell equivalent to 1 cm path length and spectral bandwidth of 1 nm was used. A standard stock solution of 10 µg/ml strength was prepared for hydralazine HCl by dissolving 10 mg drugs in a 0.1 N HCl; while by suitable dilution of the stock solution with methanol, a standard working solution of hydralazine HCl was prepared on the day of analysis. The hydralazine HCl stock solution was vigilantly diluted with 0.1 N HCl to 10 µg/ml. To detect λ_{max} for hydralazine HCl, all the samples were scanned separately in the range of 200-350 nm. The λ_{max} for hydralazine HCl was found 302 nm in thorough scanning. By using UV-VIS spectro-photometer (Thermo Spectronic UV-1, USA) at 302 nm, the absorbances of various samples were measured for drug contents [44].

Weight variation and thickness determination

From each batch, 20 tablets were sampled and accurately weighed by using an electronic single pan balance (Metlar Toledo, Switzerland) and the average weights and thickness of these tablets were calculated [31].

Hardness testing

Hardness of prepared tablets was determined by using a Monsanto hardness tester. For this purpose, 6 tablets of each formulation batches were placed in between spindle and anvil. The desired pressure required to hold the tablet in position was applied by moving the screw knob in a clockwise direction and after that, the scale was moved so that the indicator was set at zero. Then, the pressure was applied till the breaking of tablets and the reading was noted [31].

Friability testing

A friability tester USP 23 (Electro Lab, Mumbai, India) at 25 revolution/min for 4 min was used to conduct the friability test and the percent friability was determined by using the following formula [31]: % Friability = 1–F X 100/I, where, I = Initial weight and, F = Weight after friability

Swelling study

By weighing the weight of tablets at selected regular intervals, swelling study was carried out. This study was carried out in type-II dissolution apparatus, USP (Campbell Electronics, India) in 900 ml SGF (pH 1.2), which was maintained at a temperature of 37±0.5 ° C under 50 rpm paddle speed. Periodically, the swelled tablets were removed. After that, the tablets were blotted with tissue paper for drying the tablet surface and the changes in their weights were measured using single pan balance (Metlar Toledo, Switzerland) during swelling study until equilibrium was attained. To determine the equilibrium swelling (%) of these tablets, following formula was used [31]:

Equilibrium swelling (%) = $[(W_t–W_0)/W_0] \times 100$, where W_t is the weight of the swollen tablet and W_0 is the initial weight of the tablet.

***In vitro* floatation study**

By using type–II dissolution apparatus, USP (Campbell Electronics, India), *in vitro* floating ability of prepared hydralazine HCl tablets was determined. From each formulation batch, 3 tablets were placed in the dissolution vessels containing 500 ml SGF (pH 1.2) and the temperature was maintained at 37±0.5 ° C for 8 h at a speed of 50 rpm. The time required to float at the surface of dissolution medium (lag-time) and duration of buoyancy were calculated [10].

***Ex vivo* bio-adhesion study**

By using *ex vivo* wash-off method, *ex vivo* bioadhesion study was performed and for this, freshly excised pieces of goat intestinal mucosa (2 X 2 cm) was collected from the slaughterhouse. This was mounted on the stainless steel slide, connected with a suitable

support. Then on the wet and rinsed tissue specimen, the single tablet was placed and immediately after that the support was hung to the arm of the USP tablet disintegrating test machine (Campbell electronics, India). After starting of the disintegration test machine, the tissue specimen was given a slow, regular up and down movement in 900 ml SGF (pH 1.2) contained in a 1 liter vessel of the machine at a temperature of 37±0.5 °C. The time for the detachment of the test tablet from the tissue specimen was measured as bioadhesion time [31].

***In vitro* release study**

The prepared floating-bioadhesive matrix tablets of hydralazine HCl was tested for *in vitro* release by using type-II dissolution apparatus, USP (Campbell Electronics, India). Into 900 ml of SGF (pH 1.2), tablets were placed and the system was maintained at a temperature of 37±0.5 ° C under 50 rpm paddle speed.

From which 5 ml of aliquots was collected at regular time intervals by replacing the same amount of fresh dissolution medium into dissolution vessel to maintain the sink condition throughout the experiment. These collected aliquots were filtered and again diluted suitably to analyze using a UV–VIS spectrophotometer (Thermo Spectronic UV-1, USA) by measuring absorbance at λ_{max} of 302 nm [44].

Kinetic modeling of drug release

To analyze the drug release mechanism of this hydralazine HCl floating bioadhesive matrix tablets, the data of *in vitro* dissolution were fitted to various mathematical models like zero order, first order, Higuchi, and Korsmeyer-Peppas models [31, 45].

Zero-order Model: $F = K_0 t$,

First-order Model: $\ln (1-F) = -K_1 st$ t,

Higuchi Model: $F = K_H t^{½}$,

Korsmeyer-Peppas Model: $F = K_P t^n$, where F represents the fraction of drug released in time t, K_0 is the zero-order release constant, K_1 is the first–order release constant, K_H is the Higuchi dissolution constant, K_P is the rate constant and n is the release exponent. The Korsmeyer-Peppas model is usually employed to distinguish between various release mechanisms, *i.e.,* Fickian release (diffusion-controlled release), non-Fickian release (anomalous transport), and case-II transport (relaxation-controlled release).

The drug release is called Fickian, when the value of n is ≤ 0.5; while non-Fickian release is called when the n value is in between 0.5 and 1.0; when the value of n is ≥ 1.0, it is known as case-II transport [31].

Drug-polymer compatibility analysis: Fourier transform infra red (FT-IR) analysis

To assess the interaction between drugs and tablet excipients, FT-IR analysis was done. Scanning of hydralazine HCl (Pure drug), as well as powdered samples of floating-bioadhesive matrix tablets containing drug (hydralazine HCl), was done over a range of wave number 3700 to 600 cm^{-1} at a resolution of 4 cm^{-1} using a FT-IR spectrophotometer (BRUKER). The system was operated in the transmission mode.

Statistical analysis

All other data was analyzed with simple statistics using BioStat version 2009 for Windows software, AnalystSoft Inc.

RESULTS AND DISCUSSION

Drug content

Drug contents of all these cashew gum-HPMC K4M tablets containing hydralazine HCl were within the range of 97.06±3.87 to 99.90±2.93 % (table 2), which clearly indicated that drug contents were within 100±10 %. The specifications for drug content of the hydralazine HCl in USP [46] and IP [47] are that drug content should not be less than 90 % and not more than 110 %. Hence, the results of drug content ascertain the presence and compendia quality of hydralazine HCl in all these formulated cashew gum-HPMC K4M tablets.

Table 2: Physicochemical parameters of cashew gum-HPMC K4M floating-bioadhesive matrix tablets containing hydralazine HCl

Formulation codes	Weight (mg) (mean±SD; n = 20)	Hardness (kg/cm²) (mean±SD; n = 10)	Drug content (%) (mean±SD; n = 10)	Friability (%)
F1	297.48±4.12	5.17±0.42	97.06±3.87	0.11
F2	301.32±5.28	5.60±0.35	97.17±3.43	0.12
F3	300.15±3.50	6.21±0.72	99.90±2.93	0.14
F4	299.97±4.33	6.95±0.49	98.11±3.47	0.16

Weight variation and thickness

The results of weight and thickness variation of these cashew gum-HPMC K4M tables containing hydralazine HCl are presented in table 2. The weight and thickness variations act as a pointer to good manufacturing practices (GMP) maintained by the manufacturers as well as quantity of active pharmaceutical ingredient (API) present in the formulation. All the hydralazine HCl matrix tablets tested for the weight variation study showed compliance within the official specifications as none of the tablets deviated by up to 5 % from their average weight (table 2) [46, 48]. Additionally, the thickness of these cashew gum-HPMC K4M tablets containing Hydralazine HCl was found consistent.

Hardness

To evaluate the ability of tablets to withstand handling without fracturing or chipping, hardness test of all tablets were done by applying a force of about 4 kg/cm² for a satisfactory hardness of tablets [49]. All the cashew gum-HPMC K4M tablets containing hydralazine HCl were within the range, *i.e.*, between 5.17±0.42 to 6.95±0.49 kg/cm² which were shown in the table (table 2). Hence, the results of the hardness testing for all these formulated cashew gum-HPMC K4M matrix tablets of hydralazine HCl were found satisfactory.

Friability

To evaluate the tablet resistance to abrasion of tablets were evaluated by performing friability test and the compendial specifications of friability for tablets are less than 1 % w/w [46, 48]. The friability (%) of all formulated cashew gum-HPMC K4M matrix tablets of hydralazine HCl was found within the range of 0.11 to 0.16 (Table 2), indicating satisfactory friability.

Swelling

The swelling of a polymeric matrix causes dimensional changes and weight gain depending upon how much amount of water uptake occurs by the hydrophilic polymers [50]. The measurement of swelling behaviour of these cashew gum-HPMC K4M matrix tablets of hydralazine HCl was done in SGF (pH 1.2) and the equilibrium swelling (%) was within the range of 187.10 ± 6.72 to 285.55 ± 7.07 % (Table 3). Maximum swelling behaviour was shown by the matrix tablets containing higher amount of cashew gum than that of the lesser amount. It was also observed that the matrix tablets containing high amounts of hydrophilic polymer-blends (containing cashew gum and HPMC K4M) exhibited higher swelling behaviour. This fact could be attributed to higher amount of water uptake by the hydrophilic polymers present in the polymer-blends.

Table 3: Results of floating lag-time, floating duration, *ex vivo* bioadhesion time and equilibrium swelling of cashew gum-HPMC K4M floating-bioadhesive matrix tablets containing hydralazine HCl

Formulation codes	Equilibrium swelling (%) (mean±SD; n = 3)	Floating lag time (sec) (mean±SD; n = 3)	Floating duration (h)	Bioadhesion time (h) (mean±SD; n = 3)
F1	187.10±6.72	117.50±3.37	7.20	2.17±0.36
F2	237.77±8.88	33.10±1.39	12<	4.22±0.27
F3	262.48±8.53	24.47±0.88	12<	4.75±0.76
F4	285.55±7.07	13.23±0.79	12<	5.34±0.49

In vitro floatation

With minimum floating lag-time, all formulated cashew gum-HPMC K4M matrix tablets of hydralazine HCl were floated well over a long period of 12 h (table 3) as these tablets contained sodium bicarbonate as an effervescent agent. Sodium carbonate and citric acid as effervescent agents are generally able to produce CO_2 reducing the density of the matrix system, which helps to float on the aqueous medium [4-5]. In addition, buoyancy might be imparted by the HPMC K4M present in these matrixes [8]. This could produce rapid hydration and swelling of the polymeric matrices producing a floating mass in the gastric pH (1.2). With the increment of cashew gum contents in the tablet formulations, the floating lag time of this effervescent cashew gum-HPMC K4M matrix tablets of hydralazine HCl was found decreased. This might be attributed to the higher swelling property of cashew gum as it is a hydrophilic natural gum. With an increase of polymer viscosity, the swelling of the polymeric chains of cashew gum and HPMC K4M might be enhanced. However, the highly viscous polymers formed a consistent hydrogel, which might obstruct the solvent's deeper penetration into the core of the tablet matrix system. Simultaneously after a time-lag to be remained float (buoyant) in the aqueous medium, the highly swollen matrices are able to swell and lower the density of the matrices less than 1 [31].

Ex vivo bioadhesion

Besides the floating characteristics, bioadhesive tendency of these formulated floating cashew gum-HPMC K4M matrix tablets of hydralazine HCl could be beneficial for the gastro retentive drug delivery. The *ex vivo* bioadhesion onto goat intestinal mucosa was assessed in the gastric pH (SGF, pH 1.2). Again, it was also noticed that these effervescent floating matrix tablets containing a higher content of cashew gum exhibited comparatively higher *ex vivo* bioadhesion time than that of the matrix tablets containing lesser content of cashew gum (table 3). However, higher bioadhesion time was revealed by these floating matrix tablets containing a higher content of hydrophilic polymer blends (containing cashew gum and HPMC K4M) than that of the lesser content. This occurrence might be due to a more concentrated layer of the viscous gel as a result of utmost hydration as well as swelling of the matrices containing a higher amount of hydrophilic polymers [31]. Furthermore, these hydrophilic polymeric matrices could have an affinity to demonstrate bioadhesion with biological membranes by simple physical and/or hydrogen-bonding with the mucus constituents [25]. Therefore, the bioadhesive property of these formulated floating cashew gum-HPMC K4M matrix tablets of hydralazine HCl could help to stay in the GIT with increased gastro retention.

In vitro dissolution

In vitro drug release studies of these formulated floating-bioadhesive cashew gum-HPMC, K4M matrix tablets of hydralazine HCl were performed in SGF (pH 1.2) as dissolution medium. Most of these matrix tablets demonstrated sustained release of hydralazine HCl over a period of 12 h (fig. 1). Only, the matrix tablets of F1 (made of HPMC K4M without cashrew gum) release total hydralazine HCl within 8 h of dissolution. As a release retardant material, cashew gum and HPMC K4M were acted in these floating-bioadhesive matrix tablets. Slower drug release was noticed when the contents of cashew gum in these matrix tablets increased. The higher viscosity in contact with aqueous fluids of the dissolution medium (due to increased amount of cashew gum in the formula of matrix tablets) may promote the formation of highly viscous gels, which would retard the drug release rate from this floating-bioadhesive cashew gum-HPMC K4M matrix tablets of hydralazine HCl. Likewise, the elevated viscosity due to HPMC K4M contents in the formula could retard the drug release rate from these floating-bioadhesive matrix tablets. Siepmann and Peppas (2001) advocated that the drug releasing pattern from the HPMC-based matrices is regulated by these following facts [51]: (a) At the start, steep water concentration gradients are produced at the polymer-water interface ensuing imbibition of water into the HPMC-based polymeric matrices; (b) by the reason of water imbibition, swelling of HPMC-based matrices results in remarkable changes of the matrix-forming polymers, drug concentrations and rising dimensions of the matrix system; (c) upon aqueous contact, the drug dissolves and diffuses out of the matrix system because of the concentration gradient; and (d) by the increasing of aqueous content, the diffusion coefficient of the drug raises considerably. The slower drug releasing because of the increasing contents of hydrophilic polymer blends (containing cashew gum and HPMC K4M) in floating-bioadhesive cashew gum-HPMC K4M matrix tablets of hydralazine HCl could be ascribed to the formation of gel-like network obstruction at the surface of matrix tablets on immediate contact of the dissolution medium by faster swelling of the hydrophilic polymeric matrices.

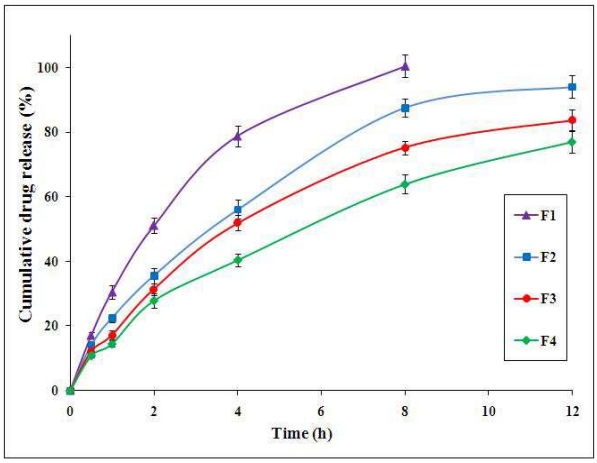

Fig. 1: *In vitro drug release from various cashew gum-HPMC K4M floating-bioadhesive matrix tablets containing hydralazine HCl in simulated gastric fluid (pH 1.2) (Mean ± SD; n = 3)*)

To investigate the drug (hydralazine HCl) releasing kinetics and mechanism of various cashew gum-HPMC K4M floating-bioadhesive matrix tablets containing hydralazine HCl in SGF (pH 1.2), the *in vitro* hydralazine HCl dissolution data were fitted to various common drug releasing kinetic models like zero-order, first-order, Higuchi and Korsmeyer-Peppas kinetic models. The results of the curve fitting into various kinetic models are presented in table 2. The hydralazine HCl releasing pattern from these cashew gum-HPMC K4M floating-bioadhesive matrix tablets was found to be correlated well with the Korsmeyer-Peppas kinetic model (R^2 = 0.9868-0.9924). The value of release exponent (n) determined from *in vitro* hydralazine HCl releasing results ranged from 0.63 to 0.67, indicating the drug release from these floating-bioadhesive matrix tablets followed the anomalous (non-Fickian) diffusion mechanism controlled by both the diffusion of drug from the matrix and release of drug through the relaxation of the matrix polymer chains.

Table 4: Results of curve fitting of the *in vitro* hydralazine HCl release data from cashew gum-HPMC K4M floating-bioadhesive matrix tablets containing hydralazine HCl in SGF (pH 1.2)

Formulation codes	Correlation coefficient (R^2)				Release exponent (n)
	Zero-order	First-order	Higuchi	Korsmeyer-Peppas	
F1	0.9095	0.7599	0.9349	0.9892	0.64
F2	0.9278	0.8028	0.9394	0.9924	0.63
F3	0.9251	0.7907	0.9214	0.9868	0.65
F4	0.9664	0.8336	0.9190	0.9919	0.67

FT-IR analysis

The drug-polymer compatibility analysis of the floating-bioadhesive cashew gum-HPMC K4M matrix tablets of hydralazine HCl was done by FTIR spectroscopy. FT-IR spectra of pure drug (hydralazine HCl) and powdered samples of F4 floating-bioadhesive matrix tablets containing hydralazine HCl were presented in fig. 2. Pure hydralazine HCl showed characteristic peaks at 3219.27 cm^{-1} (N—H stretching), 3028.47 cm^{-1} (aromatic C-H stretching), 2975.18 cm^{-1} (N-H streching). In between 2910-1675 cm^{-1} (aromatic C-H vibrations), a band was appeared in the spectra of F4 floating-bioadhesive cashew gum-HPMC K4M matrix tablets of hydralazine HCl with or without very minute shift indicating the absence of any chemical interaction between the drug (here hydralazine HCl) and the excipients employed to formulate these matrix tablets.

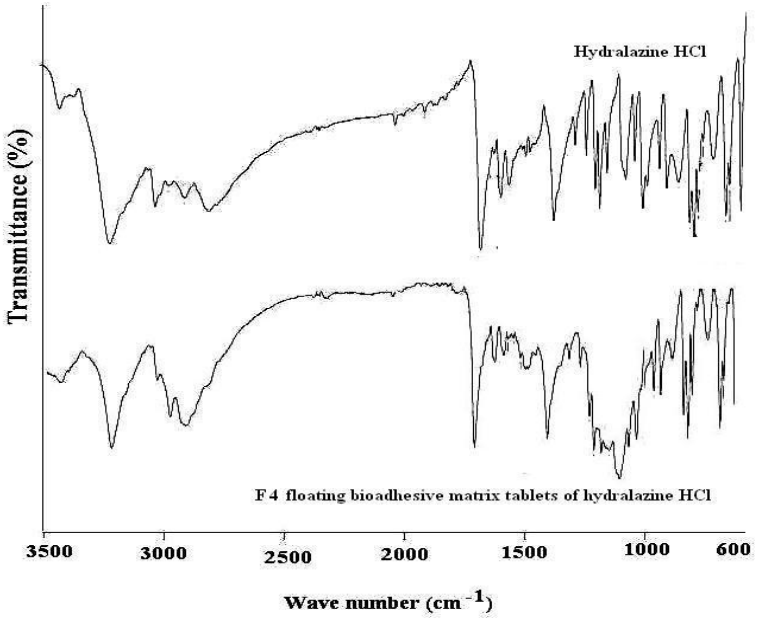

Fig. 2: FTIR spectra of pure drug (hydralazine HCl) and powdered samples of F4 cashew gum-HPMC K4M floating-bioadhesive matrix tablets containing hydralazine HCl

CONCLUSION

In this study, cashew gum-HPMC K4M floating-bioadhesive matrix tablets for gastro retentive delivery of hydralazine HCl were prepared by direct compression method with the incorporation of sodium bicarbonate and citric acid as effervescent agents. Drug contents, weight variations, hardness and friability of these matrix tablets were within the compendia limits. These matrix tablets floated well over 12 h in SGF (pH 1.2) *in vitro* with minimum lag time (less than 35 sec) and also showed a good bioadhesion time (more than 4 h) onto goat intestinal mucosa in SGF (pH 1.2). All these cashew gum-HPMC K4M floating-bioadhesive matrix tablets of hydralazine HCl showed *in vitro* sustained releases of hydralazine HCl over 12 h in SGF, pH 1.2 and followed Korsmeyer-Peppas kinetic model with anomalous (non-Fickian) diffusion mechanism. Thus, the results of the current study clearly indicate a promising potential of the use of cashew gum as matrix forming a material with HPMC K4M to prepare matrix tablets for gastro retentive delivery of hydralazine HCl through the combined approach of floatation and bioadhesion to reduce the dosing rate with better patient compliances.

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AUTHORS CONTRIBUTION

All authors of the current manuscript contributed equally

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