

DESIGN AND CHARACTERIZATION OF OROSLIPPERY BUOYANT TABLETS FOR RANITIDINE HYDROCHLORIDE

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ABSTRACT

Objective: The goal behind of performing this study was to come out with an oroslippery buoyant ranitidine hydrochloride tablet to ease the swallowing process. Hence, the drug is released controllably in the stomach regardless of the effect on gastric emptying time.

Materials and Methods: The core of the buoyant containing 150 mg of the drug was compressed directly, and sodium bicarbonate was employed as an effervescent agent, besides, hydroxyl propyl methyl cellulose (HPMC) polymer was utilized in different grades in the formulation process. The prepared core was immersed in the coating dispersion, which was formulated using xanthan gum (slipping agent) and Kollicoat instant release (IR) (for film formation). According to the variables in the formulation process, floating properties varies along with the release profile of the drug; therefore, investigation of the effects of variables was conducted, including polymer type and concentration in the core part, and the effect of Kollicoat IR amount as well as the level of coating.

Results: According to this study, it was clearly obvious that T4 formulation, that consisted of HPMC K4M, after being dipped 2 times in dispersion of 0.3% xanthan gum and 14% Kollicoat IR, had provided an instant floating, moreover, the *in vivo* slipperiness was quite acceptable as well as the taste masking. Nevertheless, the percentage of drug release measured after 6 h was 90.15%.

Conclusion: The resultant formulas is quite promising to take the lead as new approach to easy swallowing tablets without need of water especially for patients with swallowing problems as well as it is floating tablet that can retain the drug in gastric cavity to be continuously released to ensure its maximum absorption and may improve its bioavailability.

Keywords: Ranitidine hydrochloride, Oroslippery tablet, Gastro retentive, Buoyant, Kollicoat infrared, Xanthan gum.

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INTRODUCTION

Pharmaceutical industry started to persuade novel drug delivery system to optimize both safety and efficacy of the drug, through formulation the drug into a convenient dosage form. Oral dosage form has profound manifestation of inconveniency from swallowing point of view especially for pediatrics, elderly, disabled or bedridden and psychiatrists, resulting in patient noncompliance hence ineffective therapy, which falls into the need to develop various tablet dosage forms to avoid this problem. The drugs are administered via the oral route without the aid of chewing or prior dispersion/dissolution in water so a systemic effect can be produced [1,2]. So far, oroslippery tablets (OSTs), a new tablet dosage form, had been developed to avoid dysphagia as well as optimizing the traditional tablet dosage form, this dosage form relays on hydration of the tablet inside the oral cavity which offers slipperiness easily of an intact tablet without water aid, moreover, it provide taste masking through the same concept [3].

Ranitidine hydrochloride (RHCl), an H₂-receptor blocker that reduces gastric acid secretion (stimulated by histamine, gastrin, and cholinomimetic agents), as raw material it has a bitter taste and sulfur-like odor. In general, it is prescribed in the management of duodenal ulcer, gastric ulcer, and gastroesophageal reflux disease as well as erosive esophagitis. The latter condition requires about 150 mg of ranitidine 4 times a day. While administering 150 mg of the drug, conventional dose, the gastric acid secretion is inhibited up to no more than 5 h, while administering 300 mg can cause plasma fluctuations; accordingly, a sustained release dosage form is more preferred [4]. As ranitidine has a short biological half-life, about 2.5-3 h, had urged the development of a sustain release formula. Ranitidine is solely absorbed

from the initial part of the small intestine with a resultant absolute bioavailability of 50% of the administered dose [5].

New formulations have been developed to provide gastro retentive drug delivery, such as floating drug delivery, those are of low-density system that possesses an adequate buoyancy to float over the gastric contents to remain for prolonged time in the stomach regardless to the gastric emptying rate. The floating system provides the required condition to retain the drug within the cavity, therefore improving the sustained delivery of drugs given orally, that have a particular absorption window at a particular location on the gastrointestinal tract (GIT).

Those systems aid in continuously releasing of the drug prior it reaches its absorption window, so an optimal bioavailability can be achieved, moreover, the local delivery increase the bioavailability at the receptor site in the stomach, therefore, increase the efficacy of the drug by reducing the acid secretion [6].

The aim of this study was to develop a novel strategy by application of a slippery coat over intragastric core buoyant tablet of RHCl for easily swallowing process, good taste masking, high efficacy and controlled release that may lower dose, and improve bioavailability so to achieve a better compliance and can be used as alternative for the conventional non-coated tablet of the same drug.

MATERIALS AND METHODS

Materials

RHCl was provided by (Bio-technology Co., Ltd.), HPMC (K4M, K15M, K100M) (Provizerpharma, India), Kolicort IR, (Sigma Chemical Co.,

(Aldrich), USA), xanthan gum, Avecil, NaHCO₃, citric acid, mannitol, and magnesium stearate (Samara Drug Industry, Iraq). Peppermint oil and talc (Himedia, India). All other chemicals, solutions and reagents used were of analytical grade.

Methods

Preparation of the OSTs

Preparation of buoyant core tablet

The composition of different formulations of RHCl buoyant core tablets is shown in (Table 1). The tablets were prepared by direct compression method. RHCl, polymer (HPMC of different grades), gas generating agent (sodium bicarbonate), and diluent (microcrystalline cellulose) were weighed separately and passed through sieve no. 0.36. The active ingredient and excipients except the talc and magnesium stearate were mixed together for 15 min in a plastic container, the remaining ingredients were added to the previous mixture and mixed for extra 2 min. The final blend was compressed directly into tablets of average weight 400 mg using a single punch tablet of a die size 11 mm and compression force 8 [7].

Preparation of the aqueous slippery coating

The aqueous coating dispersion prepared in three steps:

Step 1: Preparation of the xanthan gum

The slipperiness inducing agent, xanthan gum (xan) [8], was added to a 40°C preheated distilled water while being mixed using magnetic stirrer at 600 rpm speed for 5 min.

Step 2: Preparation of the Kollicoat IR solution

Kollicoat IR was added gradually to mannitol containing aqueous solution with continuous stirring. Mannitol was used as a sweetening and flavor agent [9]. Stirring was conducted using magnetic stirrer at 100 rpm for 15 min at room temperature until a clear solution was formed.

Step 3: Preparation of the coating mixture

Aqueous dispersion of xanthan gum (Step 1) was added to the polymeric solution (Step 2) and mixing together using magnetic stirrer at 400 rpm for 5 min at room temperature, then peppermint oil and talc (anti-adherent and distributing agent) were added with continuous stirring at 400 rpm for extra 5 min at room temperature. Peppermint oil has a role of flavoring and cooling agent [10]; which further enhances patient compliance, also enhances the swallowing process through salivation process [11]. All constituents of the coating dispersion are shown in Table 2.

Coating RHCl core tablets

Buoyant OSTs of RHCl were prepared by dipping the core buoyant tablet (F6 which has optimum release rate and acceptable lag time as compared to other buoyant formulas) in each of the slippery coating solutions (S1, S2, and S3) using a suitable forceps, thereafter drying at 60°C by applying a hot air dryer for about 5 min (this procedure applied again to the dried single coated OSTs when double OSTs coating was

prepared), Different OSTs prepared by immersing the core in different coating dispersion types and made different coating layers to study the effect of types and number of the coating layer on the release profile of the drug, floating lag time (FLT) and *in vivo* slipperiness, and the taste masking effect of the OSTs. The composition of the RHCl OSTs is shown in Table 3.

Evaluation of the compressed tablets (before and after coating)

Physical properties

Prepared tablets were assessed for weight variation, tablet thickness and hardness, uniformity of dosage units, and friability.

The weight variation test was conducted by weighing 20 random tablets individually, calculating the average weight thereby comparing the individual weights to the average.

The hardness of each batch of tablets was measured in terms of kg/cm², where five tablets from each formula were tested through Monsanto hardness tester, and then the average reading±standard deviation (SD) was documented [12].

On the other hand, the friability test was conducted by placing 20 pre-weighed tablets in the friabilator; the latter was operated at 25 rpm for 4 min; the dust was brushed off the tablets and reweighed. Tablets to be acceptable should lose a maximum of no more than 1% of their weight. Nevertheless, the thickness of each 10 tablets was measured with the Vernier Caliper [13,14].

Determination of percent drug content (content uniformity)

The content uniformity test of the tablets was done by weighing and powdering ten randomly sampled tablets from each formulation, and individually estimated for RHCl content after solubility in sufficient volume of 0.1N HCl, via detection through UV-VIS spectrophotometer at 314 nm [15].

In vitro buoyancy study ([FLT] and total floating time [TFT])

The FLT can be defined as the time required by the tablet to be emerged on the surface of the dissolution medium, and the time the tablet constantly float on the medium surface is known as TFT as evaluated in a dissolution vessel filled with 900ml of 0.1 N HCl (pH 1.2) previously set at 37±0.50°C at 75 rpm, for both core and coated tablets [16].

In vitro release study

The *in vitro* release rates of ranitidine from slippery buoyant tablets formulas (F4-T6) (n=3) were estimated via dissolution apparatus II (paddle method) [8]. The dissolution test was done using 900 ml of 0.1 N HCl, at 37±0.50°C at 75 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at determined time intervals (15, 30, 60, 120, 180, 240, 300, and 360 min) with the replacement of the sample with 5 ml fresh dissolution medium. The samples were filtered through a 0.45-μ membrane filter. Absorbance of these solutions was measured at 314 nm using a UV/Vis- spectrophotometer. Thereafter cumulative percentage, drug release was calculated by pre-determined equation obtained from a calibration curve [17,18].

Table 1: The composition of ranitidine buoyant core tablets

Formula code mg	F1	F2	F3	F4	F5	F6	F7	F8
RHCl	150	150	150	150	150	150	150	150
HPMC K4M	160	160	160			80	100	120
HPMC 15M					80			
HPMC 100M				80				
Avecil	64	44	24	84	84	84	64	44
Na HCO ₃	20	40	60	80	80	80	80	80
Talc	4	4	4	2	2	2	2	2
Mg stearate	2	2	2	4	4	4	4	4

RHCl: Ranitidine hydrochloride, HPMC: Hydroxyl propyl methyl cellulose

Table 2: Composition of the coating dispersion (% w/w)

Ingredients	S1 (%)	S2 (%)	S3 (%)
Kollocoat IR	9	14	19
Xanthan gum	0.3	0.3	0.3
Mannitol	2.5	2.5	2.5
Talc	2	2	2
Peppermint oil	0.5	0.5	0.5
D.W	Up to 100	Up to 100	Up 100

Table 3: Composition of ranitidine slippery coated buoyant tablet

Formula code	Composition
T1	F6 (S1)
T2	F6 (S1)*2
T3	F6 (S2)
T4	F6 (S2)*2
T5	F6 (S3)
T6	F6 (S3)*2

*2double layer coating

Variables studied on the prepared formulas*Effect of effervescent agent on in vitro buoyancy properties*

Formulas F1, F2, and F3 which contain 20 mg, 40 mg, and 60 mg of sodium bicarbonate, respectively, were utilized to study the influence of the amount of effervescent agent on floating properties of core tablets.

Effect of different polymer grade

Formulas (F4, F5, and F6) were utilized to study the effect of different polymer grades (HPMC K100M), HPMC K15M, HPM CK4M, respectively, on the floating properties and Drug release of core tablets.

Effect of polymer amount

Formulas (F6, F7, and F8) were prepared to study the influence of polymer amount on the floating properties and drug release of RHCl Core tablet in which formulas F6, F7, and F8 contain HPMC K4M 80 mg, 100 mg, and 120 mg, respectively.

Effect of Kollicoat IR concentration in the coat of OSTs

Formulas T1, T3, and T5 were planned to design to study the effect of changing Kollicoat IR concentration 9%, 14%, and 19 %, respectively, on floating properties and release.

Effect of coating level on floating property and release

Formulas T1, T2, T3, T4, T5, and T6 were examined to demonstrate the effect of coating level on the floating property and release by dipping (single layer coating and double layer coating) on floating property and drug release.

In vivo evaluation of slipperiness and taste masking effect

All the *in vivo* evaluations tests were approved by the Ethics Committee of the College of Pharmacy, University of Mustansiriyah.

The evaluation of *in vivo* slipperiness was applied to the core tablet (F6) and OSTs formulas T1-T6, five healthy humans had volunteered to perform the test after gaining their full consent, the seconds required for the tablets to become slippery and swallowed whole without the aid of water was recorded and considered as an indicator for slipperiness degree.

To assure that the prepared OSTs remained intact with adequate taste masking during their residence in the oral cavity, the taste masking effect was performed using the rolling method [19] on the selected OSTs

formulas T1-T6 and F6 (core tablet) on five healthy human volunteers whom got detailed briefing on the purpose of this test. The volunteers were told to roll the tablet gently in their oral cavity without chewing or biting; whenever a slight taste of bitterness can be detected the volunteered were informed to spit the tablet out along with the saliva and to rinse their mouth immediately. The time required for bitterness sensation was recorded and considered as an indicator for taste masking property for the prepared RHCl OSTs [3].

Statistical analysis

The results of the experiments were given as a mean values \pm SD and were analyzed according to one-way analysis of variance (ANOVA) at which results considered significant when ($p < 0.05$) and non-significant when ($p > 0.05$).

RESULTS AND DISCUSSION**Evaluations of the prepared core and coated buoyant OSTs**

The prepared core tablet formulas (F1-F8) were evaluated for their physical properties, including hardness, friability, weight variation, drug content, and thickness, the results in Table 4 showed a non-significant difference ($p > 0.05$) between the prepared core tablets in their physical properties, with high tablet hardness (5.7 ± 0.73 kg/cm²) and lower friability value (0.34%). Furthermore, physical properties for the prepared RHCl buoyant OSTs are illustrated in Table 5. They showed non-significant differences ($p > 0.05$) in the hardness between the prepared in additions, non-significant differences were observed between the core and coated tablet hardness, indicating that the slippery coating had no significant influence ($p > 0.05$) on the core tablet hardness. All the prepared OSTs had an acceptable, non-significant difference ($p > 0.05$) in friability with a slight enhancement for coated tablets which resulted from higher coating thickness in double T2, T4, and T6 comparing to monolayer coating in T1, T3, and T5 consequently.

Preliminary trail (F1-F3) was prepared to study the effect of amount of effervescent agent on floating property, the results of floating properties were shown in Table 6, as the amount of NaHCO₃ increased, the FLT was decreased noticeably, this manner can be attributed to the fact that as the concentration of NaHCO₃ increases the result of effervescence amount increases as well, which lead to formation of pores, which lead to rapid hydration of the HPMC K4M polymer matrix, therefore, reducing tablet floating time. Although all prepared formulas showed a TFT more than 24 h, these three preliminary formulas were excluded from further studies, as they required a long time to float on the surface of the medium. HPMC in large concentration (160 mg) 40 % of total tablet weight acts as a gelling and matrix forming agent, it has the ability to form strong mesh-like structure after contact with the dissolution media and thus slows down the release of CO₂ (which had formed by reaction of NaHCO₃ with dissolution medium) leading to increase in FLT [20].

The effect of polymer grade on FLT was studied in which F4, F5, and F6 contain HPMC K100M, HPMC K15M, and HPMC K4M, respectively, as the viscosity of the polymer increased, the FLT increased significantly ($p < 0.05$) this can be attributed to increase tablet integrity and formation of a stronger gel layer with increasing the polymer viscosity, thus more time is required to hydrate the tablet [21].

Fig. 1 shows the effect of polymer grade on drug release in which as the grade of the polymer changed (K100M in comparison with K15M and K4M), the rate of drug release was decreased significantly ($p < 0.05$). This behavior may be elucidated by the relation between the polymer viscosity and the disentanglement concentration (the critical concentration of the polymer below which the polymer chains separate and detach from a qualified matrix). The higher polymer viscosity makes greater chain entanglement, so it becomes harder for longer chains to dissolve. This lead to the formation of thicker gel and the ability to hold the liberated gas for a longer time, and not allow the fast diffusion of the drug from the tablet matrix [22,23].

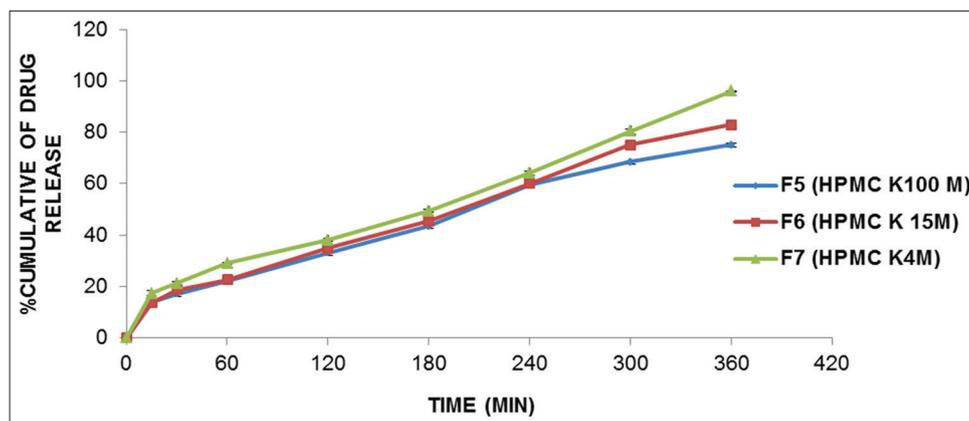


Fig. 1: Effect of HPMC grade on *in vitro* drug release of buoyant core tablet for ranitidine HCl in 0.1 N HCl solution at 37±0.5°C, (n=3) (mean±standard deviation)

Table 4: Physical properties of the prepared buoyant core tablets

Formulas	Hardness (kg/cm ²)	Weight variation (mg)	Thickness (mm)	Friability (%)	Drug content (%)
F1	5±0.56	385.2±0.83	4.1±0.38	0.35±0.03	94.5±0.09
F2	5±0.43	376.1±0.77	4.3±0.28	0.34±0.63	95±0.05
F3	5±0.33	388.9±0.68	4.3±0.08	0.36±0.6	93.5±0.03
F4	5±0.06	389±0.44	4.8±0.67	0.75±0.45	97.6±0.03
F5	4.9±0.03	395±0.54	4.6±0.08	0.62±0.5	98.3±0.33
F6	4.9±0.27	398±0.30	4.2±0.83	0.68±0.56	99.6±0.1
F7	5.5±0.8	396±0.40	4.3±0.33	0.38±0.63	94.6±0.63
F8	5.7±0.73	398±0.55	4.3±0.76	0.35±0.03	99.5±0.02

Physical properties data represented by mean±SD (n=3). SD: Standard deviation

Table 5: Physical properties of the prepared OSTs

Formulas	Hardness (kg/cm ²)	Weight variation (mg)	Thickness (mm)	Friability (%)	Drug content (%)
T1	4.9±0.02	425.4 ±0.50	4.30±0.03	0.36±0.03	98.4±0.09
T2	4.8±0.2	443.2 ±0.41	4.41±0.53	0.28±0.02	97.6±0.02
T3	4.8±0.05	426.4±0.32	4.33±0.05	0.33±0.02	95±0.2
T4	4.9±0.03	444.1±0.01	4.46±0.33	0.28±0.03	99.5±0.089
T5	4.7±0.31	428.1±0.42	4.36±0.8	0.27±0.01	99.1±0.05
T6	4.8±0.23	446.2±0.54	4.48±0.11	0.23±0.03	96.4±0.55

Physical properties data represented by mean±SD (n=3). SD: Standard deviation, OSTs: Oroslippy tablets

Table 6: FLT and TFT for prepared RHCl tablet

Formula code	FLT in seconds	TFT in hours
F1	420±0.05	>24
F2	333±0.5	>24
F3	254.4±0.3	>24
F4	43±0.23	>24
F5	39±0.1	>24
F6	26±0.02	>24
F7	20±0.09	>24
F8	18±0.02	>24
T1	77.4±0.33	>24
T2	Instant floating	>24
T3	Instant floating	>24
T4	Instant floating	>24
T5	110±0.07	>24
T6	Instant floating	>24

The results of FLT and TFT for prepared RHCl tablets (F1-F6) for core tablets and (T1-T6) for oroslippy tablets represented by mean±standard deviation (n=3). FLT: Floating lag time, TFT: Total floating time, RHCl: Ranitidine hydrochloride

The effect of polymer amount on FLT was studied in formulas F6, F7, and F8 which contain 80,100 and 120 mg, respectively, of HPMC K4M,

as the amount of polymer increased there was a decrease in FLT this may be due to the fact that increasing the amount of polymers caused rapid formation as well as entrapment of CO₂ gas into the hydrophilic polymeric gel which eventually resulted in reduction of FLT [24].

The effect of polymer amount on drug release is shown in Fig. 2, in which as the amount of polymer in the formula increased, the rate of drug release decreased significantly (p<0.05). This is due to the fact that higher polymer amount will form a stronger viscous gel layer that decrease the rate of water diffusion into the floating tablet matrix, which cause a decrease in drug release [25].

Formulas T1, T3, and T5 were planned to design to study the effect of different Kollicoat IR concentration in the coating layer (9%, 14%, and 19%), respectively, on FLT and drug release. These formulas showed an increase in FLT except T3 (Table 6) which showed an instant floating this may be related to the hydrophilicity and permeability of polymeric film for dissolution medium that results in rapid initiation of CO₂ gas accompanied with matrix swelling forming a gel layer with which air is entrapped around the tablet core after contact with gastric fluid, after the outer gel layer is eroded, the swelling boundary is moving toward the dry core, maintaining hydration and buoyancy of the system.

There was a non-significant decrease ($p>0.05$) in drug release as the concentration of coating Film polymer increased for T1 and T3 as seen in Fig. 3 while for higher concentration 19% (T5) there was a significant decrease ($p<0.05$) in drug release since Kollicoat IR is hydrophilic film former polymer and this will lead to increase the rate and extent of water uptake by water-loving core polymer (HPMC) thus leads to formation of swollen gel matrix that leads to a retardation in drug release [26].

Doubling the coating layer as in formulas T2, T4, and T6 resulted in instant floating this is may be related to the high permeability of Kollicoat IR. From Fig. 4, it was noticed that there is non-significant

decrease ($P>0.05$) in drug release when comparing the single layer coated formulas T1, T3 with their double coated counterparts T2 and T4, respectively, while T6 showed a significant decrease ($P<0.05$) in drug release in comparison to T5 this is may be related to coating thickness as the coating layer was doubled the thickness of diffusion pathway for the solvent to pass resulting in slower drug release [27,28]. As showed in Fig. 5.

In vivo slipperiness and taste masking effect of the prepared OSTs
Concerning the results of *in vivo* slipperiness for (core tablet F6) and T1-T6 (coated tablet), Fig. 6 showed that the coated tablet had

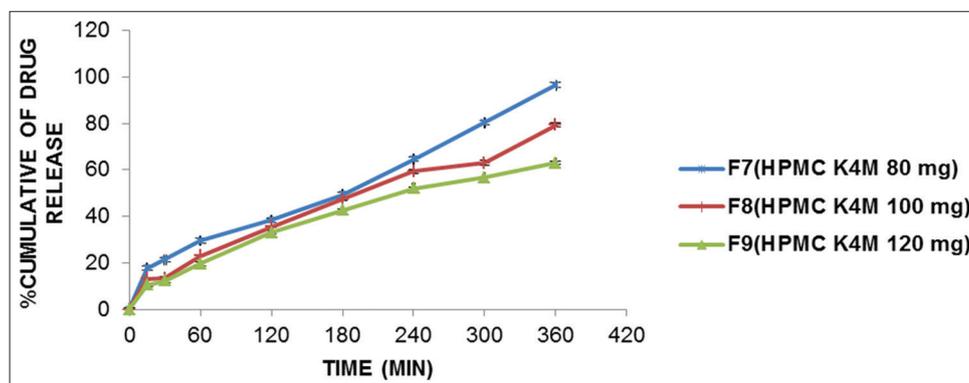


Fig. 2: Effect of HPMC K4M polymer amount on *in vitro* drug release of buoyant core tablet for ranitidine HCl in 0.1 N HCl solution at $37\pm 0.5^{\circ}\text{C}$, (n=3) (mean \pm standard deviation)

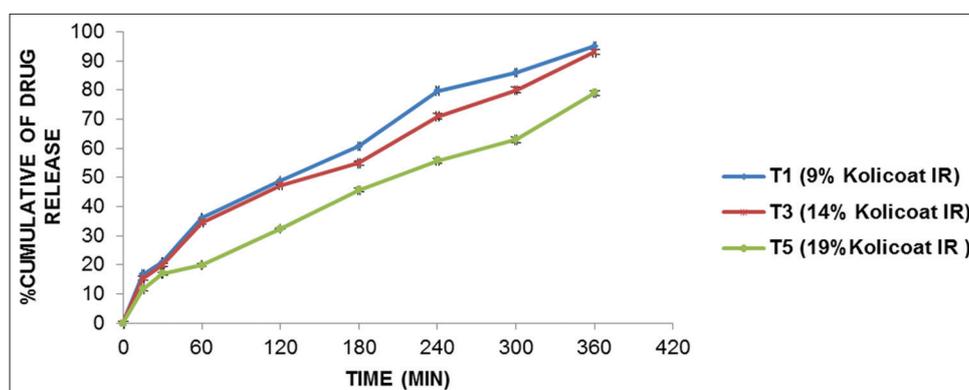


Fig. 3: Effect of increasing Kollicoat IR concentration of coat dispersion on *in vitro* drug release of ranitidine oroslippery tablet in 0.1 N HCl solution at $37\pm 0.5^{\circ}\text{C}$, (n=3) (mean \pm standard deviation)

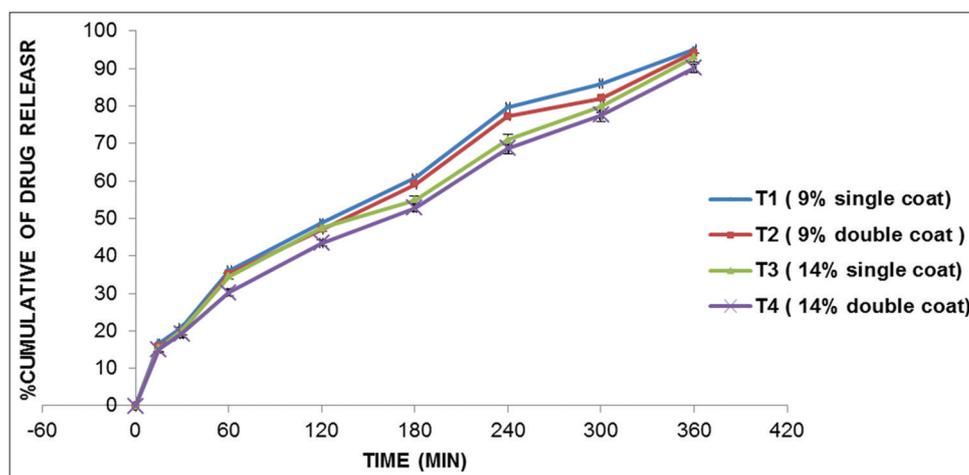


Fig. 4: Effect of coating layer level of (Kollicoat IR 9% and 14%) on *in vitro* drug release of ranitidine oroslippery tablet in 0.1 N HCl solutions at $37\pm 0.5^{\circ}\text{C}$, (n=3) (mean \pm standard deviation)

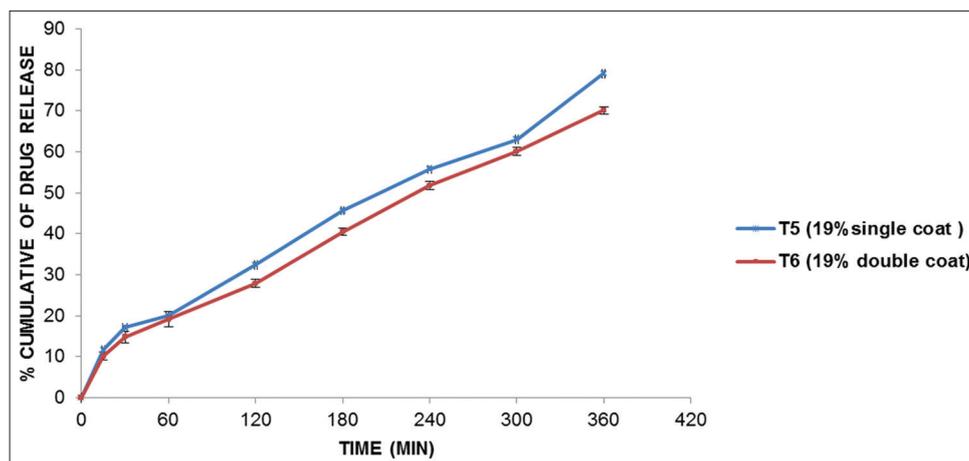


Fig. 5: Effect of coating layer level of (Kollicoat IR 19%) on *in vitro* drug release of ranitidine oroslippery tablet in 0.1 N HCl solutions at 37±0.5°C, (n=3) (mean±standard deviation)

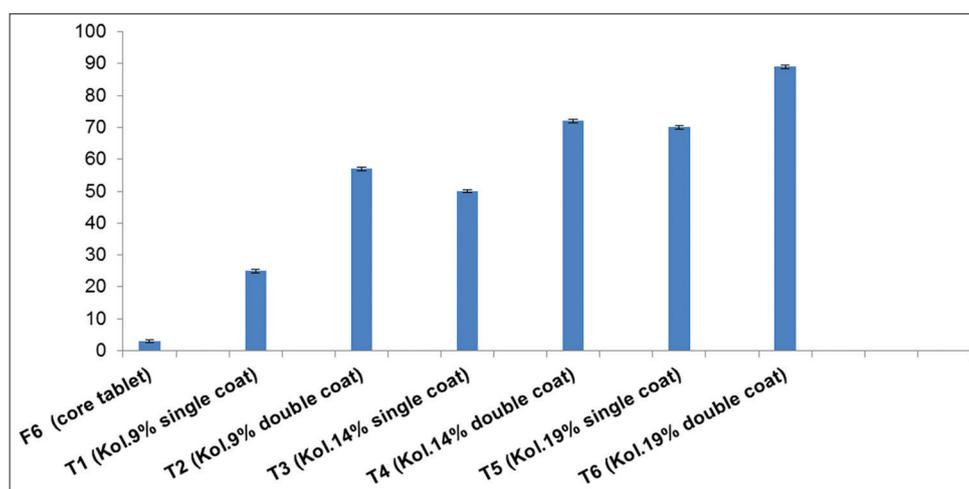


Fig. 6: The result of *in vivo* slipperiness test for ranitidine hydrochloride buoyant core and oroslippery tablets represented by mean±standard deviation (n=3), F6 shown no slipperiness

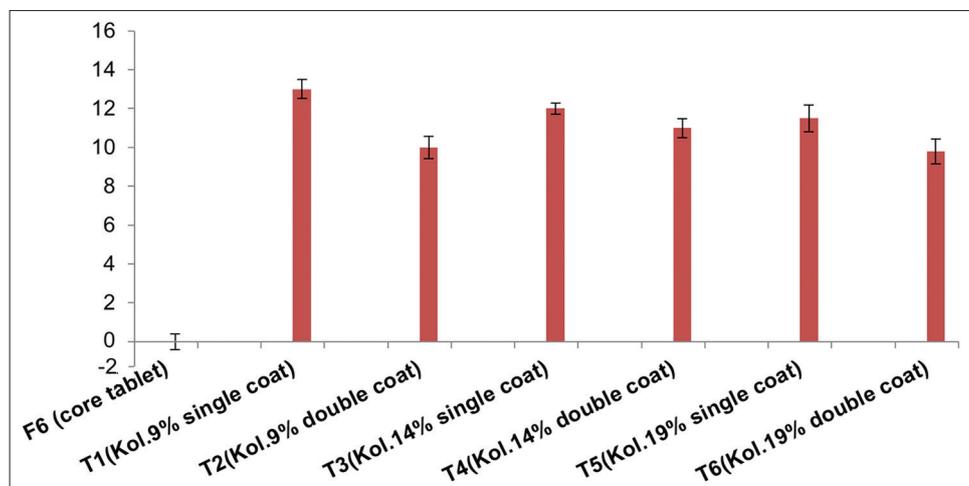


Fig. 7: The results of *in vivo* taste masking test for ranitidine hydrochloride buoyant core and oroslippery tablets, represented by mean±standard deviation (n=3)

significant effect on the *in vivo* slipperiness property, this may be due to the presence of xanthan gum in the coat which considers as slipperiness inducing agent to facilitate the swallowing process.

In addition, increasing the concentration of Kollicoat cause a non-significant increase ($p > 0.05$) in the degree of slipperiness, while the results of a double coating showed enhancement of the slipperiness,

these observations might be attributed to increase the viscosity of the coating formula up on increasing the polymer concentration [27].

The results of *in vivo* taste masking for RHCl OSTs formulas T1-T6 and core tablet F6, (Fig. 7) revealed that a significant increase in taste masking in coated tablets (T1-T6) than the non-coated core tablet, because coating the tablet created a physical barrier between the drug and taste buds, In addition, the use of mannitol and peppermint oil resulted in a fine sweet taste, sense of coolness and freshness within the mouth [29,30]. Furthermore, the results showed a significant increase ($p < 0.05$) in taste masking at the higher concentration of Kollicoat IR represented in T5 (19% Kollicoat) comparing to T1 with (9% Kollicoat) and T3 with (14% Kollicoat), in addition the results showed that double coating which represented in T2, T4, and T6 formulas, have a significant improvement ($P < 0.05$) in the *in vivo* taste masking effect comparing to monolayer coating in T1, T3, and T5, respectively, these results might be due to the greater viscosity of the coating dispersion that observed by the higher Kollicoat concentrations in T6 which increased the hydrodynamic drag of the coating dispersion that finally gave a higher coat thickness [3].

CONCLUSION

Intragastric buoyant tablet of RHCl which coated with slippery coat can be successfully prepared and optimized, this type of tablet dosage form overcomes swallowing obstacles for certain population who experienced difficulty of swallowing, provide a good taste masking and meanwhile release the drug continuously in the stomach enhancing drug absorption and bioavailability. The results of *in vitro* evaluation to study the effect of coating types and the level of coating on RHCl buoyant core tablet on the release profile, FLT and *in vivo* slipperiness and taste masking test concluded that T4 has the optimum results, a promising release rate, an instant floating, an accepted slipperiness and taste masking effect. The results of RHCl buoyant OST formulations provide a positive impact for such a newly developed approach to tablet dosage form.

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