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CURCUMIN COMPLEX EMBEDDED IN FLOATING BEAD FOR GASTRIC LOCAL TREATMENT

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Summary

Curcumin Complex Embedded in Floating Bead for Gastric Local Treatment

Curcumin, the main bioactive agent from *Curcuma longa*, is traditionally well-known for the prevention and treatment of peptic ulcers. However, low solubility and pH sensitive property limit the effectiveness of curcumin. Hence, the combination of the complexation technique with floating particles was investigated to improve the peptic local therapeutic performance of curcumin. Curcumin complexes were simply fabricated by grinding method with β-cyclodextrin and Poloxamer 407/PVP K30. Gastro-retentive floating drug delivery systems (GRDDS) were prepared from alginate and hydroxypropyl methylcellulose by the inotropic gelation method. Curcumin complex was evaluated for solubility as well as spectroscopic methods such as FT-IR, and PXRD. Curcumin GRDDS was investigated for swelling, floating behavior, and drug release. The resulting curcumin complexes containing 10% Poloxamer 407 significantly increased the solubility and dissolution rate of curcumin at pH 1.2. Moreover, the optimized curcumin gastro-retentive floating drug delivery system showed nearly 90% drug release in simulated gastric fluid and maintained 99% buoyance of floating beads after 24h. Hence, the curcumin complex embedded in a floating drug delivery system can be considered as a potential medication for gastric local treatment.

Keywords: *Curcumin, β-cyclodextrin, Inclusion complex, Curcumin gastro-retentive floating drug delivery system, Inotropic gelation.*

1. Introduction

Peptic ulcer disease (PUD) is a common disease that gastroenterologists and first care providers have encountered for several years. To be more specific, peptic ulcers are the induction of acid lesions in the stomach and duodenum. The second reason for peptic ulcer disease is *Helicobacter pylori (H. pylori)* infection in the digestive system. Moreover, the increasing use of over-the-counter acid-suppressing medications and greater caution with non-steroidal anti-inflammatory drugs (NSAIDs) are likely the third reason and also affect the stomach mechanism negatively.

Curcumin, a natural yellow-orange polyphenol extracted from the rhizome of the herb *Curcuma longa* (Turmeric), is a well-known traditional medicine remedy for ulcer stomach. Related studies expressed potential bioactivities of curcumin on likes: anti - *Helicobacter pylori* [1], anti-inflammatory [2], antioxidant [3], induction of attenuation of gastric mucosal injury caused by NSAIDs [4], anti-apoptotic in inflamed intestinal epithelial cells [5], autophagy and apoptosis modulation [6] for gastric ulcer treatment. However, curcumin belongs to group four: low solubility, low permeability in the biopharmaceutical classification system for oral administration [7], and instability in the gastrointestinal tract due to pH sensitivity [8], which limit the absorption of curcumin. Many attempts have been made to improve the solubility and stability of curcumin [9],[10],[11], and the inclusion complex with cyclodextrins (CDs) is one of the effective methods to overcome the limited bioavailability of curcumin. Curcumin complexation with β-cyclodextrin (β-CD) was proposed as a structure of one molecule of cyclodextrin combined with two curcumin molecules in its hydrophobic cavity to enhance interaction between drug-β-CD in the gastrointestinal environment. Moreover, the addition of surface active chemicals [12] or wetting agents [13] also supports the improvement of curcumin solubility in the complex formulation.

Following oral administration, curcumin is pH-sensitive and degradable in the intestinal environment. Besides, with the contraction of the digestive system, curcumin quickly leaves the stomach, resulting in a small quantity reaching the local peptic ulcer. Hence, gastroretentive drug delivery systems (GRDDS) were fabricated to solve these problems [14]. To be more specific, the floating dosage form is designed with low-density multiple unit floating beads to prolong gastric retention and control the sustained release, which is retentive in the stomach for a longer time than the conventional dosage form. This principle supports to enhance absorption, retard drug release, and reduce dosing usage for the treatment of peptic ulcers. GRDDS provides high

drug stability in gastric fluid, drug entrapment efficiency, and reduces daily dose, which protects the drug from the negative effects of gastrointestinal factors [15]. Various GRDDS have been used to improve the therapeutic efficacy of drugs that have a narrow absorption window, are unstable at alkaline pH, and are active locally in the stomach [16]. Therefore, GRDDS should be employed to provide an almost complete release of curcumin at the local gastric site and protect curcumin from pH degradation for better therapeutic effectiveness of this bioactive compound on gastric ulcers. However, major studies on GRDDS focus on the CO_2 generating mechanism, which may increase the acidic environment in the stomach [17],[18].

Although popular for gastric sore application, especially for chronic gastritis conditions, curcumin has drawbacks such as low solubility, permeability, pH sensitivity, short half-life, rapid metabolism rate, prompt elimination, and clearance from the body, which leads to limitation of orally administered bioavailability. To overcome those limits of curcumin, in this study, the combination of curcumin and β-CD complexation is applied for water-soluble enhancement in gastric fluid, also highly increasing absorption of curcumin within the human body. Moreover, encapsulation of curcumin complex in floating beads supports sustained release and site-specific dissolution of curcumin in the stomach. Moreover, this carrier makes it possible to cover pain in mucosa directly and protect curcumin from pH degradation. Therefore, in order to improve curcumin medication for ulcer treatment in the stomach, the fabrication of floating beads loading inclusion complex of curcumin with β-CD would be investigated (*Fig.1*).

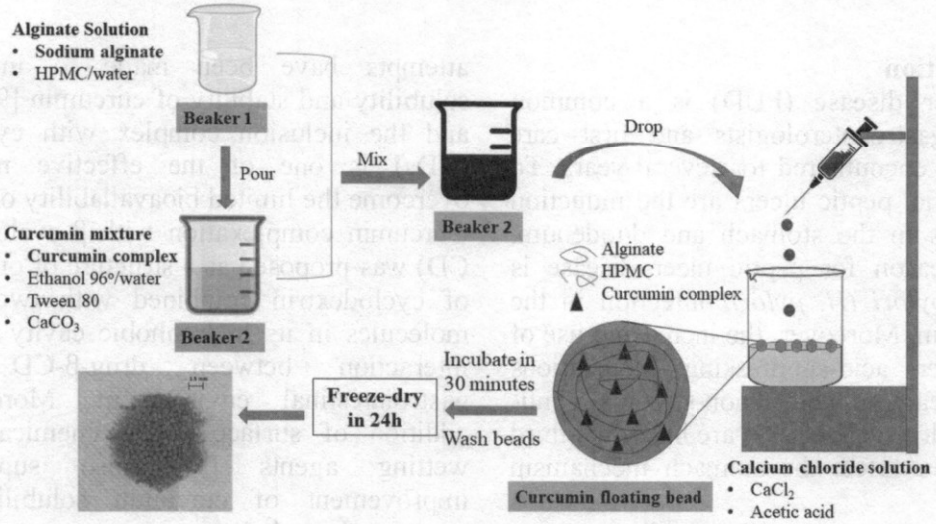

Fig. 1. Floating bead-loaded curcumin complex preparation

2. Materials and methods

2.1. Materials

Curcumin analytical grading (95% purity), β-CD from Roquette (France), Poloxamer 407 (P407) from BASF, sodium alginate (SA), calcium chloride dihydrate ($CaCl_2.2H_2O$), calcium carbonate ($CaCO_3$) analytical reagent from Guangdong Guanghua Sci-Tech Co., Ltd (China), acetic acid, Tween 80 and ethanol were purchased from Xylong Company (China), polyvinyl pyrrolidone K30 (PVP K30), hydroxypropyl methylcellulose K15M (HPMC K15M) and hydroxypropyl methylcellulose K4M (HPMC K4M), sodium dodecyl sulfate (SDS) from Sigma Aldrich.

2.2. Method:

2.2.1. Preparation and characterization of curcumin complex:

2.2.1.1. Preparation of curcumin complex:

Curcumin complex was prepared with different molar ratios of β-CD. P407 or PVP K30 was added at various ratios (w/w) into curcumin-β-CD complexes. Initially, curcumin was grinding with β-CD with ethanol 50° in the mortar and pestle. Then P407 or PVP K30 was added to mortar and grinding to obtain a homogenous paste. Finally, the paste was dried and stored in a desiccator [19].

2.2.1.2. Solubility test of curcumin complex:

The solubility of curcumin complexes was determined at pH= 1.2 at 37 ± 0.5°C. The excessive amount of each complex sample and pure curcumin are separately added into glass bottles in a shaking Julabo TW20 water bath at a speed of 100 for 24 hours. The supernatant was collected and analyzed by UV- vis spectrophotometer at 430 nm.

2.2.1.3. FT-IR analysis:

The FTIR spectra of curcumin, β-CD, P407, and the optimized complex formulation were obtained using Fourier transform infrared spectroscopy - Bruker Vertex 70 FT-IR spectrometer, with 256 scans at a resolution of 4 cm^{-1} The scanning range was 4000 and 400 cm^{-1}. The samples were ground with spectroscopic grade potassium bromide (KBr) powder and pellets were made to perform the measurements [20].

2.2.1.4. P-XRD analysis:

The X-ray diffraction of curcumin, other materials, and the optimized complex formulation was recorded using a diffractometer (Brucker D8 Advance, USA), operated at a voltage of 40 KV and a current of 40 mA. The samples were investigated in the 2θ angle range of 5-55° and the process parameters were set as: scan step size of 0.02°, scan step time of 17.7 s [20].

2.2.2. Preparation and characterization of curcumin gastro-retentive floating beads:

2.2.2.1. Preparation of curcumin gastro-retentive floating beads:

Curcumin floating beads were fabricated by an ionotropic gelation technique. Firstly, SA solution (3% w/v) was prepared by swelling SA in hot water, then adding various ratios of HPMC (4KM and 15KM) to SA solution. Secondly, curcumin was added to a solution of water, ethanol, and Tween 80, then $CaCO_3$ was added into this mixture. Next step, pour the SA solution into the curcumin mixture and stir to eliminate the air bubbles. The final mixture is dropped through a syringe with a 23G needle (0.6414 mm inner diameter) into the $CaCl_2$ solution (2% w/v) containing acetic acid (10% v/v) to obtain floating beads with agitation using a magnetic stirrer for 30 minutes. Then, wet floating beads are incubated in a $CaCl_2$ solution to improve mechanical strength in 30 minutes. After that, the wet floating beads are collected and washed in distilled water in triplicate, then freeze-drying for storage [14].

2.2.2.2. Drug entrapment efficiency and drug loading capacity evaluation:

First, 50 mg bead was dispersed in 10 ml of citric buffer solutions with pH 5.2 [21]. Then, a gentle addition of 10 ml of absolute ethanol was applied to the suspension and stirred on magnetic stirrer IKA C-MAG HS 4 at a speed of 500 rpm continuously for one hour to completely dissolve curcumin released from beads. After sufficient dilution with ethanol 50°, the curcumin content was analyzed using a UV/visible spectrophotometer at a wavelength of 430 nm for actual drug content. Drug loading capacity and entrapment efficiency were calculated by following equations below:

$$Loading\ Capacity\ (LC) = \frac{Actual\ drug\ content}{Total\ weight\ of\ bead} x100$$

$$Entrapment\ efficiency\ (EE) = \frac{Actual\ drug\ content}{Theoretical\ drug\ loaded\ in\ bead} x100$$

2.2.2.3. Floating behavior evaluation:

The floating lag time is evaluated by the time when beads are added to simulated gastric fluid (pH=1.2) and until beads begin to float on the surface of gastric fluid. 100mg beads were placed in 900 ml of HCl 0.1N containing 0.1% w/v SDS with condition at 37 ± 5°C, stirrer at 100 rpm in 24 hours. After that time, the buoyant beads are separated from the settled beads, and both the fractions of beads are dried and weighed.

$$Buoyance\ (\%) = \frac{Mass\ of\ floated\ beads}{Total\ mass\ of\ beads} x100$$

2.2.2.4. Swelling behavior evaluation:

The swelling ratio of floating beads containing curcumin complex and blank beads is evaluated by the weight of swollen beads and dried beads. 100 mg beads were placed in 900 ml of HCl 0.1N containing 0.1% w/v SDS at 37 ± 5°C, using paddle apparatus 2 at a speed of 100 rpm in 24

hours. Then, the dried beads were obtained by drying the swelling beads. The following equation is the fraction between swollen beads and dried beads.

$$Swelling\ index\ (\%) = \frac{(Weight\ of\ swollen\ beads - Weight\ of\ dried\ beads)\ x\ 100}{Weight\ of\ dried\ beads}$$

2.2.2.5. Sustained drug release evaluation:

The curcumin dissolution from the floating bead was conducted with paddle apparatus, in 900 ml of 0.1 M HCl with 0.1 % w/v SDS (pH 1.2), at 100 rpm and 37 ± 0.5°C. At 0, 0.5, 1, 4, 8, 12, 16, 20, and 24 h, a 10 ml sample was collected, and the same amount of fresh medium was substituted to preserve the sink condition. Samples were filtered and measured by UV-Vis spectrophotometer at 430 nm.

2.3. Statistical analysis

The ANOVA analysis was used to determine the statistical significance between formulations in data of evaluations. The p-value was achieved at less than 5%, which indicated a significant difference. All evaluating process was conducted in triplicate.

3. Result & Discussion

3.1. Evaluation of curcumin-β-CD complex

3.1.1. Solubility test:

The solubility of different curcumin-β-CD complexes in pH=1.2 was indicated in *Table 1*. The sample Complex 3 with a molecular ratio (1:2) between curcumin and β-CD showed the highest solubility compared with others. Specifically, Complex 3 increased around 10-folds while other samples only at 2 to 3 µg/ml, especially pure curcumin, just below 2 µg/ml. Therefore, complexation with β-CD improved the solubility of curcumin significantly, and curcumin: β CD at a ratio of 1:2 - Complex 3 was the optimal formulation for further studies.

Table 1. Solubility of various curcumin complexes

Sample	Curcumin (mol)	β -CD (mol)	PVP K30	Poloxamer 407	Solubility (µg/ml)
Pure curcumin	-	-	-	-	1.19 ± 0.09
Complex 1	2	1	-	-	2.25 ± 0.30
Complex 2	1	1	-	-	3.08 ± 0.20
Complex 3	1	2	-	-	*10.56 ± 0.42*
IC1	1	2	2%	-	9.04 ± 1.50
IC2	1	2	5%	-	10.40 ± 1.85
IC3	1	2	10%	-	17.81 ± 2.90
IC4	1	2	-	2%	23.22 ± 1.50
IC5	1	2	-	5%	30.99 ± 3.00
IC6	1	2	-	10%	*50.87 ± 1.50*

Formulations IC1, IC2, IC3 were curcumin-β-CD complex with PVP K30 at ratio 2%, 5% and 10% w/w and IC4, IC5, IC6 were curcumin-β-CD complex with P407. In combination with PVP K30, IC3 containing 10% PVP K30 increased the solubility of curcumin by around 15-folds at pH=1.2. On the other hand, IC6 loading 10% Poloxamer 407 enhanced the highest solubility of curcumin approximately 42-folds at pH=1.2 compared with pure curcumin, which is presented in Table 1. With an amphiphilic structure composed of a hydrophobic block (POP) between two hydrophilic units (POE), P407 could form chemical bonds with lipophilic drugs, disperse effectively in solvents, and improve the solubility of drug [22]. Consequently, the curcumin-β-CD complex contained Poloxamer 407/PVP K30 improved the solubility of curcumin considerably, from 10 to over 40 folds. Especially, IC6 with curcumin-β CD at a ratio of 1:2, and 10% w/w P407 was a promising formulation for further research.

3.1.2. FT-IR analysis:

In FTIR evaluation, every specific chemical bond in the investigating sample is represented by the appearance of a particular wavelength range. The appearance or existence of a peak indicates the specific chemical interaction of drug-excipient or excipient-excipient. FTIR spectroscopy was used to determine the formation of the curcumin-β-CD complex containing Poloxamer 407. *Fig.2a* indicated the FTIR spectra of curcumin, β-CD, P407, and IC6 (10% P407) to analyze the chemical interaction. The pure curcumin FTIR spectrum expressed the strong absorption band in the crystalline spectrum at 3600-3200 cm^{-1}, which indicated the presence of the phenolic O-H stretching vibration. Besides that, the stretching

vibration of the cyclic alkene (benzene ring) of curcumin was at 1576 cm^{-1} and vibrations of the C-O and C-C group were at 1509 cm^{-1}. The FTIR spectrum of β-CD was ascertained in the observed band at 3172 cm^{-1} and 2907 cm^{-1}, which corresponded to -OH stretching vibration and -CH_2 group stretching vibration, respectively. Moreover, the band at 1017 cm^{-1} in the β-CD spectrum showed the stretching vibration of C-O-C. Additionally, the FTIR spectrum of P407 was observed in bands at 2877 cm^{-1} (C-H stretching aliphatic group), 1341 cm^{-1} (O-H group), and 1148 cm^{-1} (C-O stretching vibration). Besides that, the FTIR spectrum of the physical mixture also observed the stretching vibration of peaks in the spectrum of β-CD and curcumin at 1576 cm^{-1}, 1017 cm^{-1}, and 1068 cm^{-1}. Most of all above absorption peaks in pure curcumin and the P407 spectrum decreased the transmittance or disappeared in formulation IC6 (10% P407). Specifically, in the FTIR spectrum of IC6, all absorption peaks of β-CD could be found, however, all characteristic peaks of pure curcumin almost disappeared. Especially, vibration of the C-O and C-C group at 1509 cm^{-1} was observed to determine the formation of curcumin - β-CD in the inclusion complex. This interaction agreed with a previous study, in which curcumin - β-CD complexes were fabricated by the co-precipitation method [20]. Hence, the interaction between curcumin and excipients such as β-CD and P407 remained curcumin in the amorphous form to increase solubility and dissolution rate of curcumin from complex, as well as limited the mobility of curcumin in this combination for improving curcumin complex stability.

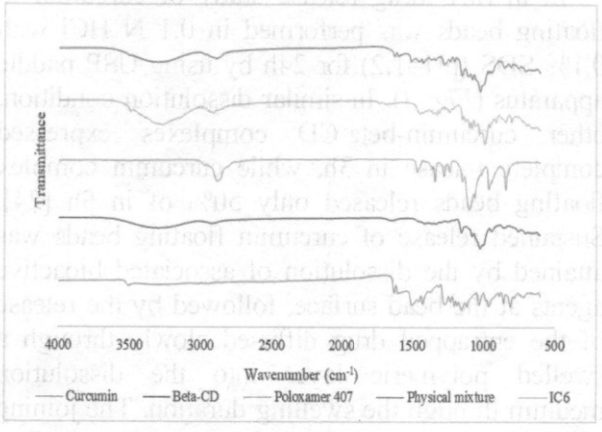

Fig. 2a. FT-IR spectra of optimum curcumin complex and materials

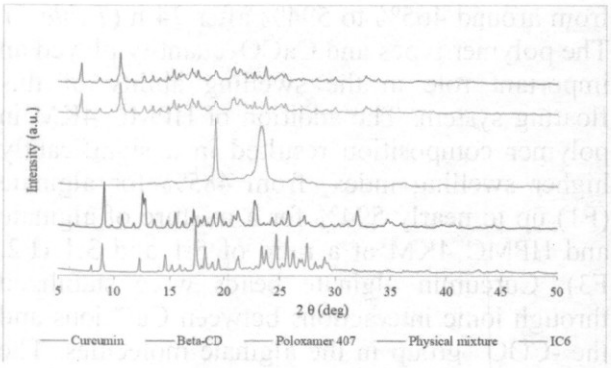

Fig. 2b. Powder X-ray spectra of optimum curcumin complex and materials

Fig. 2. FT-IR and PXRD spectra of optimum curcumin complex and materials,
2a FTIR, 2b PXRD

3.1.3. PXRD analysis:

The PXRD spectra of curcumin, β-CD, P407, and IC6 (10% P407) were shown in *Fig. 2b*. In these line graphs, some sharp peaks of curcumin at the diffraction angle (2θ) were shown at ranges at 7.94°, 8.95°, 12.27°, 14.59°, 17.33°, 18.22°, 24.70°, 25.69°, 27.45°, which suggested that the powder existed in a crystalline form. The XRD pattern of β-CD presented at ranges of the diffraction angle (2θ) at 8.95°, 12.27°, 14.59°, 17.33°, and 18-29°. Additionally, P407 showed two main peaks of the diffraction angle at 19.25° and 23.43°. Moreover, the pattern of the physical mixture appeared two highest peaks of the diffraction angle at 9.08°, 22.91° which indicated the peak of pure curcumin and β-CD. However, in the pattern of formulation IC6, the sharp peaks of β-CD at 8.95°, 12.27°, 14.59, and 18-29° showed lower intensity than the physical mixture. The diffractogram of IC6 only performed some weaker peaks of β-CD and pure curcumin that confirmed the encapsulation of curcumin in β-CD molecule as the formation of the inclusion complex. Moreover, the two main peaks found in P407 disappeared in the case of sample IC6. Consequently, the PXRD result of IC6 indicated the successful formation of curcumin inclusion complex, as well as the amorphous form existence of curcumin for better solubility and dissolution of this bioactive compound.

3.2. Curcumin gastro-retentive floating drug delivery system

3.2.1. Swelling and floating performance:

The swelling behavior of floating beads in release ensures that beads have high media entrapment and do not pass through the pyloric sphincter. Curcumin beads had a swelling index

from around 465% to 594% after 24 h (*Table 2*). The polymer types and $CaCO_3$ quantity played an important role in the swelling ability of this floating system. The addition of HPMC 4KM in polymer composition resulted in a significantly higher swelling index, from 485% for alginate (F1) up to nearly 594% for a mixture of alginate and HPMC 4KM at a ratio of 5:1 and 3:1 (F2, F3). Curcumin alginate beads were stabilized through ionic interactions between Ca^{2+} ions and the $-COO^-$ group in the alginate molecules. The combination with HPMC 4KM loosened the rigidity of the calcium alginate matrix, and enlarged the pore size among polymers, leading to higher swelling behavior of curcumin floating beads through the capillary mechanism. In cases of blended HPMC K15M, even using SA:$CaCO_3$ at a ratio of 1:1, the swelling index was only slightly more than 430%, considerably lower than alginate beads, which indicated that polymer types strongly affected the swelling ability of curcumin floating beads.

Table 2. Properties of curcumin floating beads

Chemicals	SA: HPMC	SA: $CaCO_3$	EE (%)	Buoyancy (%)	Swelling index (%)
F1	-	1:1	65.13 ± 2.48	96.17 ± 2.47	485.46 ± 23.62
F2	5:1	1:1	72.71 ± 1.40	98.58 ± 0.96	*593.94 ± 73.16*
F3	3:1	1:1	70.20 ± 2.69	98.41 ± 0.53	*593.64 ± 41.35*
F4	3:1	1:0.75	78.10 ± 3.73	98.32 ± 0.84	577.03 ± 38.52
F5	3:1	1:0.5	80.99 ± 3.28	79.03 ± 1.90	464.72 ± 32.87
F6	5:1	1:1	74.35 ± 2.16	99.80 ± 0.71	433.13 ± 36.81

Noted: only F6 using HPMC 15 KM, instead of HPMC 4KM in other formulations

Besides, the higher the quantity of gas-forming agent, the better the swelling behaviors of curcumin floating beads. At a ratio of SA: $CaCO_3$ of 1:0.5, the swelling index was only more than 460%, compared to approximately 600% at a ratio of 1:1 of SA:$CaCO_3$. This could be explained by the greater porous structure inside the beads, which was formed by the reaction of $CaCO_3$ and CH_3COOH during the preparation of curcumin floating beads and was maintained throughout the freeze-drying process. Drying methods greatly alter the porosity structure of floating beads, as buoyancy and swelling index were just around 23% and 20%, respectively, in oven drying. The freeze-drying method provided a porous structure to widen the interacted surface between the beads and the medium, enabled the osmolarity of the medium into the polymer matrix, and ensured the retention time in the stomach as well as the release ability of bioactive agents [14].

All samples immediately floated on the surface when contacting the medium, so the floating lag time would be considered as zero. Moreover, curcumin floating beads attained a high buoyance, nearly 100% in simulated gastric medium after 24h, except for F5 which consisted lowest amount of gas forming agent, which is considerably higher than 90% of floating curcumin beads in another study [23]. The high floatation of beads enhanced the high gastro-retentive probability of avoiding passing to the small intestine.

3.2.2. Curcumin entrapment efficiency and release:

Almost all the curcumin floating beads had high entrapment efficiency (EE), around 80% (*Table 2*), and LC in the range of 4-6%. The polymer combination and gas-forming agent - $CaCO_3$ affected to EE and LC of curcumin floating beads. Specifically, the inclusion of HPMC increased EE by enhancing the pore size and pore quantity in the beads, while the decrease in $CaCO_3$ ratio also boosted their EE.

In *in-vitro* drug release study of curcumin in floating beads was performed in 0.1 N HCl with 0.1% SDS (pH=1.2) for 24h by using USP paddle apparatus (*Fig. 3*). In similar dissolution condition, other curcumin-beta-CD complexes expressed complete release in 3h, while curcumin complex floating beads released only 50% of in 5h [24]. Sustained release of curcumin floating beads was attained by the dissolution of associated bioactive agents at the bead surface, followed by the release of the entrapped drug diffused slowly through a swelled polymeric layer into the dissolution medium through the swelling duration. The joining of HPMC 4KM in curcumin bead matrix as well as the quantity of gas-forming agent were responsible for curcumin release performance.

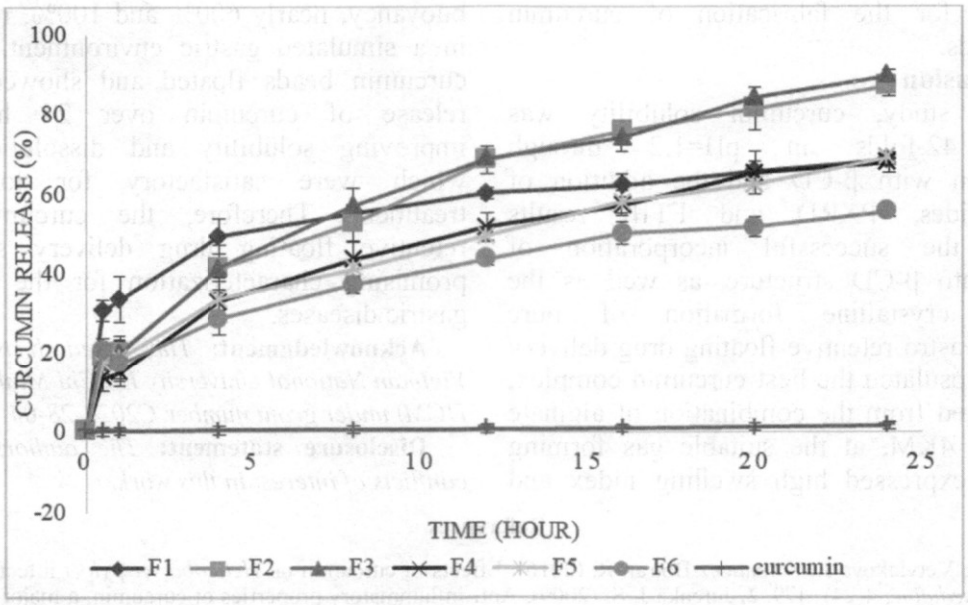

Fig. 3a. *In vitro* curcumin release profile of curcumin floating beads

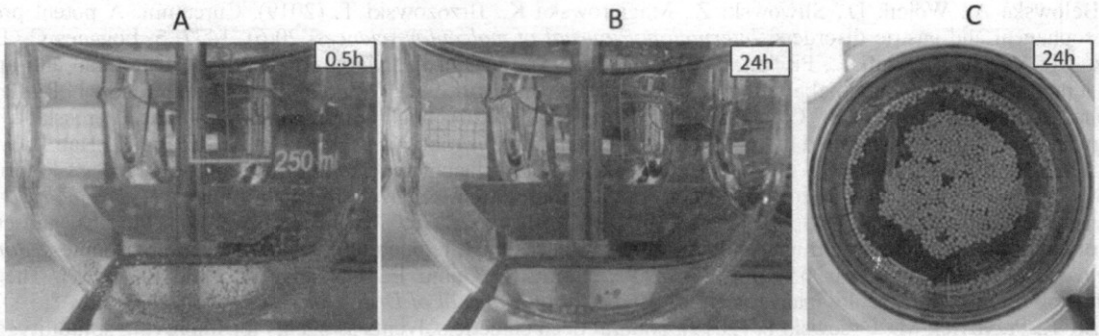

Fig. 3b. Images of curcumin floating beads release over 24 hours - A) and B) Drug release at 0.5h and 24h, C) floatation at 24h

Fig. 3. Release performance of curcumin floating beads

At 30 min point, alginate beads (F1) the showed highest percentage of curcumin release, more than 30%, considerably higher than beads formed from the mixture of alginate and HPMC 4KM, (F2 - F5) only around 15%. Besides, the porous size of incorporated HPMC beads was larger than in alginate ones due to crosslinker CaCl2. After 24 hours, curcumin beads from the combination of HPMC 4KM and alginate with the largest amount of $CaCO_3$ (F2, F3) achieved the highest percentage of drug release, around 90%. Beads formed at lower gas forming quantities as SA: $CaCO_3$ of 1:0.5 and 1:0.75 (F4, F5), around 70% of curcumin diffused into the medium after 24h. Finally, the sample containing only alginate (F1) had the lowest rate, as about 50% of curcumin dissolved at the endpoint. Using HPMC 15KM (F6), floating beads expressed sustained release, as 40% curcumin dissolved after 24 hours, which is completely adverse effect compared to HPMC 4KM [25].

Besides, in another research, the curcumin alginate floating beads with prepared with ethanol, cremophor RH40, Tween 20, PEG 400, and Labrasol [23]. In the comparison of two types of alginate as well as M-rich, and G-rich, the sample containing M-rich alginate gave a higher drug release than G-rich alginate in pH=1.2 at 8h. Moreover, the sample of floating beads combined with 1% curcumin, 2% G-rich alginate, 1% foam powder, 10% peppermint oil, 10% Cremophor RH40, and 10% ethanol that achieved the highest release drug around 35% at 8h in pH 1.2, which is significantly lower than curcumin release at the same point in this study.

Based on the curcumin release profile of different floating beads, the optimal formulation would be SA: HPMC 4KM at 3:1, with SA: $CaCO_3$ at 1:2, loading curcumin - β-CD complex

with P407 for the fabrication of curcumin floating beads.

4. Conclusion

In this study, curcumin solubility was enhanced 42-folds in pH=1.2 through complexation with β-CD and the addition of P407. Besides, PXRD and FTIR results confirmed the successful incorporation of curcumin into β-CD structure, as well as the decreasing crystalline formation of pure curcumin. Gastro-retentive floating drug delivery system encapsulated the best curcumin complex, was fabricated from the combination of alginate and HPMC 4KM, at the suitable gas forming agent, and expressed high swelling index and buoyancy, nearly 600% and 100%, respectively, in a simulated gastric environment. Moreover, curcumin beads floated and showed sustained release of curcumin over 24 hours, thus improving solubility and dissolution profile, which were satisfactory for local peptic treatment. Therefore, the curcumin gastro-retentive floating drug delivery system has promising characterization for the therapy of gastric diseases.

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