Original Article

Formulation, Development and Characterization of Microspheres of Calcium Channel Blocker

Rana Riyadh Al-ani[1], H. N. K. AL-Saman[2]

[1]Department of medical lab techniques,College of health and medical techniques, Al MAAQAL PRIVATE UNIVERSITY, Basrah, Iraq.

[2]Department of Pharmaceutical Chemistry, College of Pharmacy, University of Basrah, Basrah, Iraq.

Abstract

"AIM"- Using a new drug delivery technology, such as Nifedipine microspheres, this study sought to increase the solubility of a particular calcium channel blocker."MATERIAL & METHODS"- Quasi-emulsion diffusion is used to create floating microspheres of Nifedipine. A magnetic stirrer at 50 rpm is used at room temperature to dissolve the predetermined weighted amount of Nifedipine, ethylcellulose, "polyethylene oxide, and hydroxy propylmethyl cellulose (HPMC K15M)". Particle size, bulk density, compressibility index, and attitude of repose are used to describe the microsphere's "values beneficial in the prediction of Flowability." There has been careful pouring of the microspheres through the funnel until they are just touching the funnel's tip. "RESULTS & DISCUSSION"- The microsphere is previously arranged by removing water from the cavity of the microsphere and air drying it. In F3, F7, and F9, the percentage yield of microspheres rose with increasing ethyl cellulose concentration. The drug content was checked to ensure that the medication was uniformly placed in the microspheres during the microencapsulation method. However, mechanical factors cause the loss of the final product. Thus the procedure yield may not be 100 percent. The readings of θ varied from 25° to 29°, suggesting that the powder should have a satisfactory flow quality for the formulation. CONCLUSION- It is determined that all of the parameters for optimizing floating microspheres are found to be adequate. Evaluation of formulations' dependability under accelerated balancing situations.

Keywords: "Formulation & Characterization, Microspheres, Calcium Channel Blocker, Nifedipine, Gastric retention time.".

Introduction

The primary purpose of an oral controlled drug delivery system is to provide improved bioavailability and release of medication from the system, which should be predictable and repeatable. However, this is challenging due to physiological difficulties such as volatility in the stomach emptying process, restricted absorption window, and stability difficulty in the intestine. This may be overcome by modifying the physiological state and tailoring the formulations, by which the gastric emptying process can be extended from a few minutes to 12 h. A medicine can operate locally in the stomach in the case of H. Pylori (tetracycline) or in the proximal section of the intestine via prolonged contact with absorbing.1,2

Increased bioavailability, less waste, and increased solubility of medications that are less soluble in alkaline pH are all benefits of prolonged stomach retention. 3 Allows for a prolonged absorption phase for local medications treatment and higher bioavailability for unstable pharmaceuticals in the intestinal or colonic environment using these dosages forms. 3 Floating ion exchange resins, high-density expansion systems, magnetic systems, super porous hydrogels, raft systems, low-density systems, and mucoadhesion systems can all be used to keep food in the stomach. 3-4

Address for correspondence: H. N. K. AL-Saman
Department of Pharmaceutical Chemistry, College of Pharmacy, University of Basrah, Basrah, Iraq.
Email: hussein.khalf@uobasrah.edu.iq

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The current study's goal is to examine how to optimize drug transport architectures, namely Nifedipine microspheres. Floating homes and release profiles were optimized using a variety of formula factors.

MATERIAL and METHODS

FORMULATION OF HOLLOW MICROSPHERES 5-9

Using a modified Quasi-emulsion diffusion approach, floating microspheres with a central hole cavity are arranged. Nifedipine, ethylcellulose, polyethylene oxide, and hydroxy propylmethyl cellulose (HPMC K15M) are dissolved in a 1:1 solvent mixture of ethanol and dichloromethane at room temperature for 50 minutes in a magnetic stirrer at 50 rpm. This solvent is poured drop by drop into a hundred ml distilled water containing two ml Tween eighty at a temperature of 50 two degrees Celsius. The resulting solution is swirled for three hours at 1100 rpm with a pitched-blade impeller-type agitator to allow the hazardous solvent to evaporate. Microspheres are formed as a result of this. The microspheres are assembled using a variety of polymer ratios.

Eleven formulations are created by varying the number of ingredients, as shown in the table.

"Table 1: Formulation chart of Nifedipine hollow microspheres."

"INGREDIENTS"	"F1"	"F2"	"F3"	"F4"	"F5"	"F6"	"F7"	"F8"	"F9"	"F10"	"F11"
"Nifedipine" "gm"	"0.1"	"0.1"	"0.1"	"0.1"	"0.1"	"0.1"	"0.1"	"0.1"	"0.1"	"0.1"	"0.1"
"Ethylcellulose (gm)"	-	-	2	1	1	1	2	1	2	1	-
"Polyethylene oxide" "gm"	-	1	1	2	-	-	-	-	-	-	-
"HPMC K15M gm"	-	-	-	-	1	2	1	-	-	-	-
"Eudragit S100 gm"	-	-	-	-	-	-	-	1	1	2	1
"Solvent (ethanol) ratio (ml)"	"1:1"	"1:1"	"1:1"	"1:1"	"1:1"	"1:1"	"1:1"	"1:1"	"1:1"	"1:1"	"1:1"
"Tween 80(ml)"	2	2	2	2	2	2	2	2	2	2	2

Micromeritic properties of microsphere10-11

The microspheres have been characterized by their micrometric characteristics, such as the particle size, bulk density, and compressibility index of the microsphere's "values useful in predicting flowability."

Particle size

In the past, optical microscopic techniques were used to measure the microsphere particle size, and a calibrated ocular micrometer and stage micrometer was used to compute the suggested particle measurement.

Angle of repose

Table 4.07 explains the connection between powder float and the perspective of repose. A fixed funnel method is adopted. A funnel is then placed on a horizontal platform with its tip positioned at a specific height above the format paper. After careful pouring down the funnel, the conical pile of microspheres is just touching the tip of the funnel's spout. The pile's diameter and height were then calculated. The formula was used to compute the viewpoint of repose for the samples.

"Tan θ = Height"

"Radius"

Tapped bulk density

Tapped density testing equipment "Electrolab tapped density tester ETD-1020" and the percent compressibility index is formerly used to evaluate the tapped density of microspheres.

Compressibility (Carr's) index

Mechanical Electrolab faucet density testers determine tapped density by weighing a known amount of powder in a graduated cylinder. Samples have been tapped to the point where no further decrease in the pattern's amount could be noticed. The table shows the correlation between powder flowability and % compressibility. The formula is used to compute Carr "s index value.

"% Compressibility index = 1- V/Vo× 100"

"Where Vo and V are the volumes of the sample before and after the standard tapping."

"Table 2: Relationship between powder Flowability & % compressibility."

"% Compressibility range."	**"Flow description"**
"5-15"	"Excellent (free-flowing granules)"
"12-16"	"Good (free-flowing powder granules)"
"18-21"	"Fair (powdered granules)"
"23-28"	"Poor (very fluid powders)"
"28-35"	"Poor (fluid, cohesive forces)"
"35-38"	"Very Poor"
">40"	"Extremely poor"

Floating Characteristics

In vitro buoyancy of microspheres

Using a USP dissolving test equipment II, 100 mg of hollow microspheres were dispersed on 900 ml of 0.1 N HCl containing 0.02 percent v/v tween 80 as a surfactant and allowed to float for 24 hours. It was kept at 37°± 0.5°C for 12 hours by using a paddle revolving at 100 rpm. Microspheres were collected in two distinct batches, one for floating and one for settling. The dried and weighed microspheres were used. The following equation was used to determine the fraction of floating microspheres.

$$\text{"\% Floating capability"} = \frac{\text{"Weight of floating hollow microspheres"} \times 100.}{\text{"The initial weight of hollow microspheres"}}$$

In vivo floating behavior"12

It was done in the same way as the last treatment, except that barium sulphate was used instead of the medication. X-rays of the abdomen were obtained at predefined intervals using X-ray equipment.

In vitro drug release study 13-14

USP dissolving testing device II is used to measure the release rate of drugs from formulations (basket type). 900 cc of 0.1 N HCl and 50 to 100 rpm are used for the dissolving test at 37± 0.5 oC and 50 to 100 rpm. At regular intervals, 5 ml of the sample is taken and replaced with an equivalent volume of new dissolving media to maintain the sink conditions. PCP dissolution v2.08 software is used to fit the release kinetics into several models.

"Mechanism of drug release," 15-17

Models developed by Higuchi to explore the release of high and low water-soluble medicines embedded in semisolid or solid matrices are presented. Based on Fick "s rule, this model describes drug release as a square root of the time-dependent diffusion of the drug. It is found by determining the best fit of the data to zero order, first order, matrix (Higuchi), Hixson-Crowell, and Korsmeyer Peppas plotting of the release data. To characterize drug dissolution from various types of modified launch pharmaceutical dosage forms, this connection can be:

"Qt =K H = √t"

"where KH is Higuchi s rate constant, and Qt is the amount of drug released at time t. In these cases, a more general equation can be used. Korsmeyer et al. developed a simple, semi-empirical, about exponentially the drug launch to the lapsed time".

"Qt/ Qα =Ktn"

RESULTS & DISCUSSION

Preparation of hollow microspheres

The hole microsphere was created by blowing air into the hollow of the microsphere. Tween eighty is an emulsifying agent that adsorbs at the droplet-aqueous interface and prevents droplets from aggregating. It was previously established that adding polymer solution to water containing Tween 80 unexpectedly results in massive polymer precipitates, lowering the percentage yield of microspheres.

"Figure 1: Prepared Nifedipine hollow microspheres."

Percentage yield

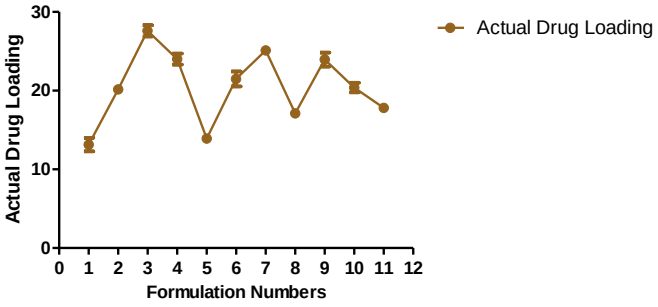
In F3, F7, and F9, it is found that the microspheres' share yield increased as the concentration of ethyl cellulose increased. There is proof of what we know in table 3. 18-20

"Table 3: Percentage yield of Nifedipine hollow microspheres."

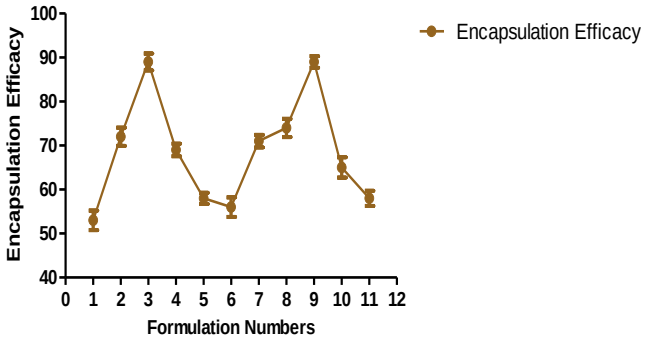
"Formulation"	"% Yield ± SD*"
"F1	"56.3±1.2"
"F2	"69.5±2.3"
"F3	"94.2±1.9"
"F4	"88.7±1.3"
"F5	"58.5±1.7"
"F6	"54.8±1.3"
"F7	"72.8±1.7"
"F8	"78.8±2.1"
"F9	"85.1±1.5"
"F10	"67.2±2.8"
"F11 "	"79.3±2.5"

Drug loading and encapsulation efficiency

The drug content test is done to ensure that the substance is evenly distributed throughout the sample. In microencapsulation, the mechanical factors contribute to the loss of the final product. Hence the method yield can no longer be guaranteed to be 100%. The size of the microspheres appears to be affected by the amount of loading. When the load is high, the proportion of big particles is also high. F3, F7, and F9 showed the best results in both drug loading and yield. 21-23



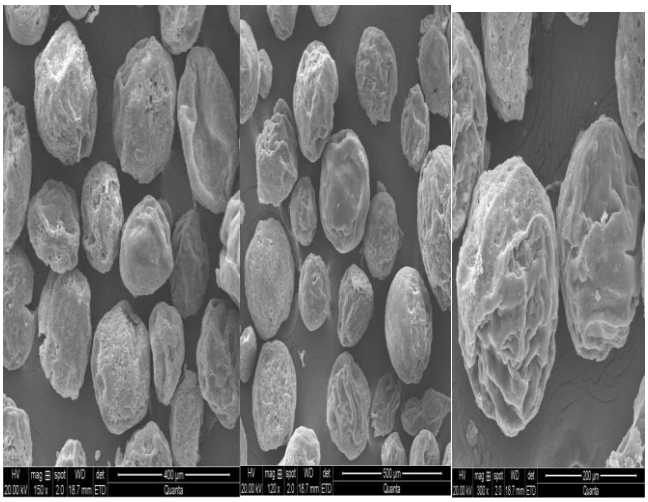
"Figure 2: Effect on Actual Drug Loading of different formulations."



"Figure 3: Effect on Encapsulation efficacy of different formulations."

Scanning electron microscopy (SEM)

Due to the rapid diffusion of solvent, some microspheres may burst. Due to the existence of a hole cavity, the microspheres floated for more than 12 hours.



"Figure 4: SEM photograph of microspheres at different magnifications."

Angle of repose

"The values of θ ranged from 25° to 29°, indicating that the got values had been properly inside the limits for the powder to have excellent drift properties. This result confirmed that the prepared hole microspheres have moderately top float properties".

Compressibility index

The price of CI is shown to range between 13.7 and 26.1 percent. The tapped density values varied from 0.138 to 0.281 g / cm3. The compressibility index results suggested that the flow qualities were true to life.

The particle size of hollow microspheres

Microspheres made from ethylcellulose, HPMC, and eudragit had a larger particle size than those made from "ethyl cellulose and polyethylene oxide ($p<0.05$)". The suggested particle dimension of the microspheres significantly increased with polymer awareness, which is consistent with

Madan MK et al. 20. Due to the rapid polymer precipitation, larger particles were generated, resulting in hardness and the avoidance of further particle dimension reduction during solvent evaporation. Additionally, the shrinking of the polymer is avoided by fast removing the solvent; this is done by gently removing the solvent. The particle measurement distribution curve of F3 is shown in the figure, and the bar format of particle measurement distribution is shown in the parent 24-26.

"Table 4: Micromeritic properties of Nifedipine hollow microspheres."

"Formulation"	"Mean size* "(μm)	Θ °*	CI%*	"Tapped density*" ("g/cm"^{3})
"F1"	"257±3.6"	"25±0.2"	"20.8±1.1"	"0.201±2.3"
"F2"	"306±3.4"	"28±1.4"	"16.2±1.6"	"0.197±3.4"
"F3"	"312±2.5"	"28±0.6"	"13.7±1.1"	"0.225±3.9"
"F4"	"308±3.2"	"28±2.8"	"18.6±2.2"	"0.166±3.7"
"F5"	"223±3.4"	"24±1.6"	"23.9±1.9"	"0.138±1.7"
"F6"	"334±2.8"	"29±1.7"	"26.1±1.4"	"0.210±4.4"
"F7"	"446±4.5"	"28±2.5"	"21.9±1.6"	"0.141±3.6"
"F8"	"347±1.4"	"28±1.7"	"25.8±1.3"	"0.228±3.2"
"F9"	"393±3.7"	"27±1.9"	"18.8±2.8"	"0.154±4.8"
"F10"	"377±4.5"	"26±2.7"	"21.7±1.2"	"0.174±3.2"
"F11"	"302±3.3"	"26±1.6"	"20.8±2.7"	"0.281±4.6"

In vitro buoyancy of microspheres.

Changing the amount or concentration of ethyl cellulose (7 cps) in different formulations was used to regulate the floating behavior. As a group, formulas 1, 3, 7, and 9 had the highest proportion of floating ability. There is a graph showing the percentage of floating in vitro results and a table of data 27.

"Table 5: In vitro % floating ability data of hollow microspheres."

"Formulation"	"% floating hollow." "microspheres"
"F1 ..	"83.1 ±1.15"
"F2 ..	"72.2±2.25"
"F3 ..	"84.4±3.56"
"F4 ..	"76.5 ±2.21"
"F5 ..	"78.1 ±1.62"
"F6 ..	"70.5±2.89"
"F7 ..	"80.8 ±3.2.1"
"F8 ..	"77.4 ±2.34"
"F9 ..	"84.9 ±2.21"
"F10 ..	"76.4±3.96"
"F11 ..	"65.3 ±3.73"

In vitro drug release studies.

The drug's release time is once extended to 12 hours. Preliminary burst release is verified in formulations F3, F4, and F11. Another possible explanation for the release of drugs from microspheres is that the drug moved to the surface with water during drying or exposed drug crystals on the surface. After one hour, the rate of medication release slows down significantly. A 12-hour in vitro Nifedipine dissolving study using electrolab dissolution equipment II was performed using floating hole microspheres of Nifedipine in a pH 1.2 hydrochloric acid buffer. There is 43.0 percent to 80.76 percent of drug release at eight hours and 75.3 to 99 percent at 12 hours ($p<0.05$) for formulations F1-F1128. It was shown that HPMC and ethyl cellulose microspheres (F5 to F7) were more stable than other combinations. HPMC's gelation feature, which produces a gel matrix upon contact with the dissolving liquid, is most likely to blame. This may be attributed to a low polymer content, which results in smaller particles with a more extensive surface area and hence a higher percentage of drug release at the end of 12 hours for F1 and F11.

Conclusions

In the current research effort, there was much focus on enhancing belly-targeted drug delivery structures, such as mucoadhesive or floating. Microspheres of Nifedipine have been created that adhere to the mucosa. It took a great deal of experimentation and optimization of many approach factors to arrive at the optimal floating homes and launch profiles. Formulations were assessed under accelerated steadiness for most of the formulations in the study.

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