International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 **ijppr.humanjournals.com** ISSN: 2349-7203

Formulation and Evaluation of a Floating Microspheres of Paracetamol

B. V. Nagarjuna Yadav*, Shubhangi N Pillewan, Pranita Bhattad, Harsh N Dalal, Ankit P Papalkar, Anisha I Vidhani, Shreyas P Tiwaskar, Shreya A Dewang.

Department of Pharmaceutics, School of Pharmacy, G.H. Raisoni University Amaravti, Maharashtra, India.

Received: 2025-4-01 Revised: 2025-4-12 Accepted: 2025-4-20

ABSTRACT:

Oral controlled release systems are designed to release the drug *in-vivo* with prediction so as to increase efficacy, minimize adverse effects and increase bioavailability of drugs. In this research work we formulated floating paracetamol microspheres and evaluated percentage drug release in body accomplish controlled drug release. Using an ionotropic gelation method, floating microspheres were created using a polymeric matrix that usually included polymers like sodium alginate. Numerous metrics, such as drug content, flow properties, Carr's index, Hausner's ratio, and in vitro drug release profiles, were used to describe the microspheres. In order to balance buoyancy and controlled release, the recipe was refined. In simulated stomach fluid (SGF), the floating microspheres showed good buoyancy, staying afloat for more than 11 hours. The drug's sustained release over a long period of time was found in the in vitro release study, which decreased dosage frequency and improved therapeutic efficacy.

Keywords: Paracetamol, Floating Microsphere, Polymeric Matrix, Inotropic Gelation Method, Buoyancy, Controlled Release, Simulated Gastric Fluid, Narrow Therapeutic window.

INTRODUCTION:

As an analgesic and antipyretic, paracetamol is utilized. It is the recommended analgesic-antipyretic substitute for aspirin (acetylsalicylic acid), especially for children, those with coagulation issues, people with a history of peptic ulcers, and those who are unable to take aspirin (American Medical Association, 1986). In 1893, paracetamol made its debut in clinical medicine. In the USA, it was first used as a prescription medication in 1951. In 1955, it was made available without a prescription (Ameer & Greenblatt, 1977). It is easily accessible without a prescription in many nations[1].

For adults, the standard oral dosage is 500–100 mg. The daily dosage should not exceed 40 mg, though it may be repeated every 4 hours if needed. The recommended dosage for youngsters is 10–15 mg/kg; no more than five doses should be given in a 24-hour period. It is advised for young children to not recommended for prolonged period (more than ten days) (Flower et al., 1985). According to the American Medical Association (1986), the standard dosage for oral and rectal administration is the same[2].

The over-the-counter drug paracetamol is an analgesic (pain reliever) and an antipyretic (medication that treats fever). In terms of pharmaceuticals, it is distinct from other over-the-counter drugs like naproxen and ibuprofen, which are similarly used to alleviate pain and fever. Acetaminophen is commonly used to treat fever and pain in children and adults. It is available as a tablet, liquid, injectable, and rectal form[3]. Acetaminophen is mainly referred to as "paracetamol" outside of the US and Canada, and it serves the same purposes. After being accidentally discovered to have antipyretic properties, acetanilide was swiftly adopted into medicine as an antifebrin (Cahn and Hepp). It was also demonstrated to have analgesic and antipyretic properties[4].

It is typically advised to adhere to the dosing instructions on the packaging of over-the-counter medications, even though the maximum daily dosage has become rather contentious in recent years. The majority of medicine dosages for kids are determined by their weight.

Dosing information on the container may be expressed in milligrams (mg) of medication per kilogram(kg) of a child's weight. The Tylenol professional product monograph states that "the recommended dose of acetaminophen for adults and children 12 years of age and older is 650 to 1000 mg every 4 to 6 hours as needed, not to exceed 4000 mg in 24 hours." Acetaminophen dosage

recommendations for children under 12 years old are 10 to 15 mg/kg every 4 to 6 hours, with a maximum of 5 doses (50 to 75 mg/kg) in a 24-hour period.

Given that there are different liquid acetaminophen concentrations for babies and kids, it is highly advised to carefully read the dosage directions and contact your child's physician with any issues regarding acetaminophen dosage[5]. More than 90% of currently available treatments are given orally, which is the most practical and preferred method of drug delivery. The first problem facing pharmaceutical businesses whenever a new chemical entity is identified is how to create a dosage form that can be taken orally with efficacy in the first place. However, frequent drug doses to maintain a steady plasma concentration and low patient compliance restrict the therapeutic efficacy of traditional oral drug delivery systems[6].

By enhancing the dose form to release the medicine gradually over a longer length of time in a controlled manner, such pharmacokinetic restrictions can be addressed. Microspheres sometimes referred to as microparticles, are one such method. A medicinal substance is delivered to the target site in a well-controlled and sustained model by a novel drug delivery system. One A free-flowing, spherical particle made of a polymer matrix and medication is called a microsphere or microparticle. They are made up of synthetic polymers or proteins that are biodegradable and have a particle size of less than 200µm. Another name for microspheres is microparticles. Microspheres had been investigated[7]. Notably for their application in the field of medication transport, and different polymers were used to produce the microspheres, which were then evaluated for diverse objectives.

Multiarticulate drug delivery systems called microspheres are made to administer drugs for extended periods of time or under regulated conditions, enhancing stability and bioavailability while delivering the medication to a specified location at a predefined pace. They are composed of natural, semi-synthetic, and synthetic polymers, as well as polymeric waxy or other protective compounds. Proteins or synthetic polymers make up microspheres, which are characterized by free-flowing powders with particle sizes between 1 and 1000µm[8].

Low-density systems with enough buoyancy to float above the contents of the stomach and stay there for an extended amount of time are known as floating systems. The medicine is delivered gradually at the desired pace while the system floats over the stomach contents, increasing the gastro retention period and decreasing fluctuations in the plasma drug concentration[9].

Microspheres are tiny, spherical particles that usually have dimensions between 1 and 1000 micrometres. A variety of synthetic and natural materials can be used to create microspheres1[0]. There are three types of commercially accessible microspheres: glass, polymer, and ceramic. Solid and hollow microspheres vary greatly in density and, consequently, are employed for different applications. Usually, hollow microspheres are added to materials to reduce their density. Floating microspheres typically refer to small spherical particles that have a lower density than the surrounding liquid or medium they are placed in, allowing them to float or remain suspended rather than sink[11,16]. These microspheres can be made from various materials such as polymers, glass, or metals and they find applications in a wide range of fields including medicine, cosmetics, and materials science[12].

Floating microspheres are sometimes referred to as hollow microspheres, microballoons, or floating microparticles. Strictly speaking, floating microspheres are spherical, coreless particles[13,17,18]. These particles, which range in size from 1 to 1000 µm, are free-flowing[14]. They used an emulsion solvent evaporation approach to create non-effervescent hollow polycarbonate microspheres[15]. With a specific density of less than one, this gastrointestinal transit-controlled product is made to float on gastric fluid.

Material and Methods:

Paracetamol, Sodium alginate and Calcium chloride was obtained as gift sample from Loba chemicals PVT. LTD.

Calibration Curve of Paracetamol.

For the stock solution, approximately 500 mg of paracetamol was accurately weighed and transferred into a 100 mL volumetric flask. About 70 mL of an appropriate solvent, such as methanol or a methanol-water mixture, was added to the flask. The flask was gently swirled or shaken to dissolve the paracetamol completely. After complete dissolution, the volume was adjusted to the 100 mL mark with the solvent. Thorough mixing was ensured by inverting the flask several times. The resulting solution had a concentration of approximately 1 mg/mL (1000 µg/mL), which served as the stock solution.

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 ijppr.humanjournals.com ISSN: 2349-7203

Table No 1: Formulation Table

Sr.no.	Ingredients	F1	F2	F3
1	Paracetamol	500 mg	500 mg	500 mg
2	Sodium Alginate	1% w/v	2% w/v	3% w/v
3	Calcium Chloride	5%w/v	5%w/v	5%w/v

Method of Preparation of Microspheres:

Formulation:

2% Sodium alginate solution: 2g of Sodium alginate was dissolved in 100 ml of distilled water. 5% Calcium chloride solution: 5g of Calcium chloride was dissolved in 100ml of distilled water.

Preparation of Micro-sphers:

The paracetamol microspheres were prepared by using ionotropic gelation method. Approximately 500 mg of paracetamol was accurately weighed and mixed into a 100 mL solution of sodium alginate using a magnetic stirrer to ensure uniform dispersion. The resulting mixture of the drug and sodium alginate was then slowly poured into a calcium chloride solution dropwise, using a syringe. This process allowed the crosslinking of the sodium alginate polymer by calcium ions, leading to the formation of microspheres. After preparation, the microspheres were collected and stored overnight in a vacuum desiccator to facilitate drying and to ensure their stability.

Fig.1: Floating Microspheres of Paracetamol (F2)

Evaluation Parameters:

Solubility:

Determine the precise weight of one gram of paracetamol. Record the amount of solvent required for full dissolution and add it dropwise while swirling until it dissolves. Where indicated, repeat the procedure at various temperatures.

Melting Point:

Select pure, dry paracetamol crystals and mill them gradually until the particles are uniform in size. Make sure the sample is distributed uniformly by filling the capillary tube to a height of roughly 2-3 mm. Start the heating program after inserting the prepared capillary tube into the device. Note the temperature at the beginning of the softening process, the start of the full melting process, and the completion of the dissolution process. For accuracy, be sure that every measurement is done three times.

Density Determination:

Bulk Density:

A weighed amount of microspheres were filled into a measuring cylinder and the volume (V_0) occupied by the microspheres were noted and the bulk density was calculated as followed:

$$\text{Bulk Density} = \frac{\text{Mass of the microsphere (W)}}{\text{Initial volume of the microsphere (Vf)}}$$

Tapped Density:

A weighed quantity of microspheres was filled in a measuring cylinder and the cylinder was tapped against a wooden surface at regular interval for 100 times, then the volume occupied by the microspheres was noted down and tapped density was calculated as followed:

$$\text{Tapped Density} = \frac{\text{Mass of the microsphere (W)}}{\text{Tapped volume of the microsphere (Vf)}}$$

Flow Properties:

Carr's Index:

Carr's compressibility index were calculated for the uncoated microspheres using the following equations:

$$\text{Carr's index} = \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \times 100$$

Hausner's ratio:

Hausner's ratio were calculated for the uncoated microspheres using the following equations:

$$\text{Hausner's ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Angle of Repose:

It is a measure of resistance to flow and calculated by funnel method. A weighed quantity of microspheres was passed through the funnel and the heap was formed on the paper. The area of the heap was encircled and diameter of the circle and the height of the heap were measured and the angle of repose was calculated as followed:

$$\text{Tan}\Theta = \frac{2H}{D}$$

Where, H = Height,

D=Diameter of Heap

$\frac{2H}{D}$ = surface area of the heap formed.

Drug Content:

A sample of microspheres containing an amount equivalent to 100 mg of paracetamol was weighed, crushed, and dissolved in 100 mL of distilled water. The mixture was stirred using a magnetic stirrer for 24 hours. After this period, a portion of the solution was

withdrawn, and analysed using a double-beam UV-Vis spectrophotometer (SHIMADZU PVT Ltd., India) at 257 nm to determine the drug content.

In Vitro-Drug Release Studies:

In vitro release studies were conducted using a USP Type II dissolution apparatus (Veego, 8DR, and India) with 900 mL of acid buffer (pH 1.2) for the first 3 hours, followed by phosphate buffer (pH 6.8) as the dissolution medium. The temperature was maintained at 37±0.5°C, with the apparatus set at 50 rpm. Microspheres equivalent to 100 mg of paracetamol were used for the study. Samples of 5 mL were taken at regular intervals, and an equal volume of fresh dissolution medium was added to maintain the volume. Each sample was appropriately diluted with the dissolution medium in the ratio of 1:1 and analysed using a UV spectrophotometer at 257 nm to determine the drug release.

Results and Discussion:

Calibration Curve of Paracetamol:

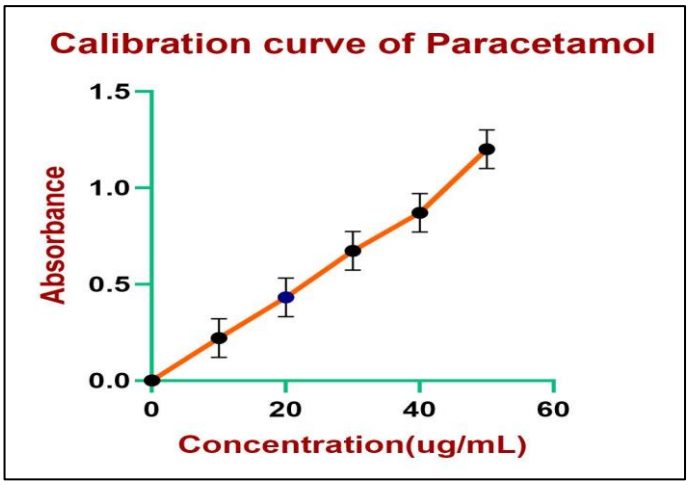

Fig No: 2 Calibration Curve of Paracetamol

Solubility Study:

Table No: 2 Results of Solubility Test

Solvent	Solubility
Water (100°C)	Soluble
Ethanol	Soluble
Acetone	Soluble
Methanol	Soluble
Propylene glycol	Soluble
Glycerol	Slightly Soluble
Chloroform	Slightly Soluble

Determination of Melting Point:

The Melting point of Paracetamol was obtained at 169^0C.

International Journal of Pharmacy and Pharmaceutical Research (IJPPR)
Volume 31, Issue 4, April 2025 ijppr.humanjournals.com ISSN: 2349-7203

Determination of Density and Flow Properties

Table No: 3 Flow Properties of Various Formulations

Sr.no.	Bulk ensity g/cm^3	Tapped Density g/cm^3	Carr's Index%	Hausner's Ratio	Angle of Repose °
F1	0.19	0.29	21.45	1.01	29
F2	0.28	0.38	26.31	1.35	34
F3	0.31	0.43	29.89	1.89	41

Drug content:

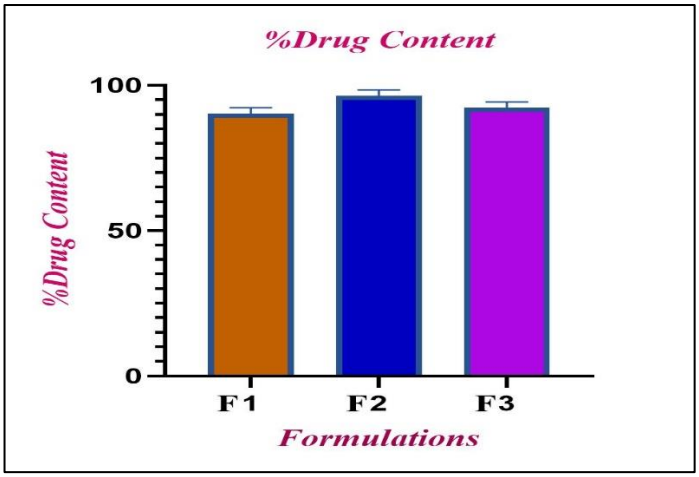

Fig No: 3 Drug content of various Formulations

In-Vitro Drug Release Studies:

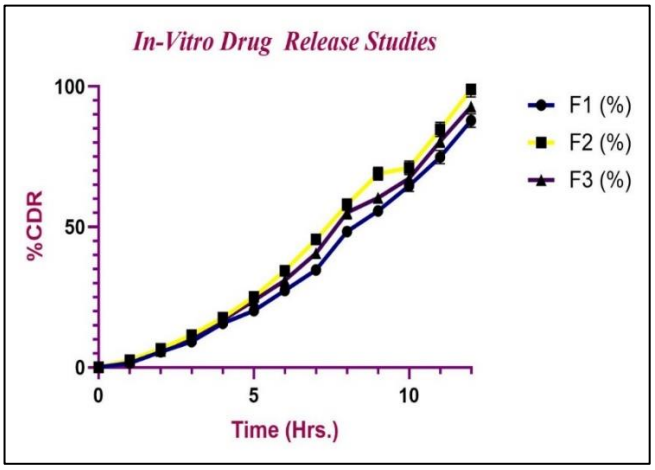

Fig No: 4 Cumulative percentage drug release of various formulations

Discussion:

Microspheres are a novel drug delivery method in which the medicine is encased in spherical structures composed of various polymers that create a matrix. Because of their great versatility, microspheres are being used in a wide range of applications, including drug administration, medical, and diagnostics. The process of medication absorption in the gastrointestinal tract is quite varied, and the duration of drug absorption is prolonged by prolonging the stomach retention of the dose form.

As gastro retentive dosage forms, floating microspheres provide for a significant improvement in healthcare by precisely controlling the target drug's release rate to a particular location. It is anticipated that improved multi-unit floating microspheres will give physicians a new option for a more affordable, secure, and bioavailable formulation in the efficient treatment of a variety of illnesses. Additionally, this study indicates that microspheres are an improved drug delivery method that can address issues with traditional dosage forms. In vitro drug release studies, density, flow characteristics, and drug content were among the evaluation metrics that were used to evaluate the produced formulations.

The prepared microspheres had shown significant densities of 0.38 and 0.28 g/cm³, respectively. When the flow parameters of the microspheres were evaluated, they displayed a Carr's Index (compressibility index) of 26.31%, an Angle of Repose of 34°, and a Hausner's Ratio of 1.35. Out of the three batches, the F2 batch had exhibited maximum drug content (96.4%). By the end of twelve hours, the maximum drug release of 98.10% was recorded. Multiarticulate drug delivery methods, such as microspheres, are therefore designed to deliver medications to a specific place at a predetermined pace while improving stability and bioavailability over long periods of time or under controlled release.

Conclusion:

Floating microspheres, as gastro-retentive dosage forms, shows significant influence on healthcare by precisely controlling the target drug's release rate to a specific region. For the efficient treatment of a variety of illnesses, optimized multi-unit floating microspheres should provide physicians a new option for a more affordable, secure, and bioavailable formulation. According to current research, microspheres are an improved drug delivery technology that can address issues with traditional dosage forms in order to increase the medication's oral bioavailability and provide controlled release over an extended period of time. According to the findings of this study, the formulation of floating microspheres increases the drug's oral bioavailability and efficacy by giving it more time to stay in the stomach and release.

REFERENCES:

1. Jouyban, A. e. (2008). Solubility Prediction of Paracetamol in Water–Ethanol–Propylene Glycol Mixtures at 25 and 30 °C Using Practical Approaches. Chemical & Pharmaceutical Bulletin, vol. 56, no. 4, 2008, pp. 602-606.
2. Development and Evaluation of Floating Microspheres. Tropical Journal of Pharmaceutical Research October 2012, 7.
3. Anamika Saxena K. (2014). Floating Microspheres as Drug Delivery System. Sciknow Publications Ltd. AJPPS 2014, 1(2):27-36, 1-11.
4. Athira K, K. V. (2022). Microspheres as A Novel Drug Delivery System - A Review. Int. J. Pharm. Sci. Rev. Res., 1-7
5. Bib Dolma Gurung, S. K. (2020). An overview on microspheres. International Journal of Health and Clinical Research, 1-14
6. Iwuozor, K. O. (2019). A Review on the Properties and Uses of Paracetamol. International Journal of Pharmacy and Chemistry,1-6.
7. Manish Dubey, P. K. (2012). Formulation and Evaluation of Floating Microsphere. International journal of pharmaceutical and chemical sciences, 10.
8. Mousami S Samanta, D. G. (2021). A review on Microspheres as a Novel Controlled Drug Delivery System. Asian Journal of Pharmaceutical and clinical research, 1-9.
9. Noopur Pandey, D. A. (2016). Formulation and Evaluation of Paracetamol. International Journal of Pharma Sciences and Research (IJPSR), 12.
10. Rerusuoghene, A. C. (2022). Solubility and Dissolution Enhancement of Paracetamol Using In Situ Micronization by Solvent Change Method. International Journal of Biosciences, vol. 21, no. 2. Shikha Kesharvani, P. K. (2019).
11. Formulation and Evaluation of Metformin Hydrochloride Loaded Floating Microspheres, International Journal of Pharmacy and Pharmaceutical Sciences, 9.
12. Vaghani S, Vasanti S, Chaturvedi K, Satish CS. Stomach-specific drug delivery of 5-fluorouracil using ethylcellulose floating microspheres. Pharm Dev Technol 2010; 15:154–61. 33. Farooq U, Khan S, Nawaz S, Ranjha NM.
13. Enhanced gastric retention and drug release via the development of novel floating microspheres based on Eudragit E100 and polycaprolactone: synthesis and in vitro evaluation. Des Monomers Polym 2017; 20:419-33. 34.
14. Choudhury PM, Kar M, Chauhan SC. Cellulose acetate microspheres as floating depot systems to increase gastric retention of antidiabetic drug: formulation, characterization and in vitro–in vivo evaluation. Drug Dev Ind Pharm 2008; 34:349–54
15. Ershad S, Sai KV, Kartheek U, Sandeep M, Prameela Rani K. Preparation and evaluation of floating microspheres of ritonavir. J Pharm Pharm Sci 2014; 3:5-11. 36.
16. Mahaveer DK, Tejraj MA. Poly (vinyl alcohol) and poly (acrylic acid) sequential interpenetrating network pH-sensitive microspheres for the delivery of diclofenac sodium to the intestine. J Controlled Release 2004; 96:9–20. 37.
17. Sharma M. In vitro and in vivo evaluation of repaglinide loaded floating microspheres prepared from different viscosity grades of HPMC polymer. Saudi Pharm J 2015. Doi:10.1016/ jsps.2015.02.013 38.

18. Dubey M, Kesharwani P, Tiwari A, Chandel R. Formulation and evaluation of floating microsphere containing an anti-diabetic drug. Int J Pharm Chem Sci 2012;1:1038-47
19. Kamel HA, Sokar SM, Gamal SS, Naggar FV. Preparation and evaluation of ketoprofen floating oral delivery system. Int J Pharm 2001; 220:13-21. 27.
20. Narasimha SDP, Murthay NL, Chowdhury P. Kinetic modelling on drug release from controlled drug delivery system. Acta Pharm 2010; 67:217-23. 28.
21. Suleiman NN. The kinetics of drug release from ethylcellulose solid dispersions. Drug Dev Ind Pharm 1985; 11:2169-81. 29.
22. Simonelli DS, Higuchi W. Investigation of factors influencing release of solid drug dispersed in inert matrices. J Pharm Sci 1965; 54:1459-64. 30. Higuchi T. Mechanism of sustained action medication. Theoretical analysis of the rate of release of solid drugs dispersed in solid matrices. J Pharm Sci 1963; 52:1145-9.

How to cite this article:
B. V. Nagarjuna Yadav et al. Ijppr.Human, 2025; Vol. 31 (4): 169-176.
Conflict of Interest Statement: All authors have nothing else to disclose.