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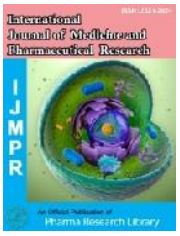

Research Article **Open Access**

Formulation and Evaluation of Valsartan Microballoons

Gowramma A*[1], A. Mounika[2], A. Vinod babu[2], P. Ratna kala[2], B. Prathibha[2], E. Susanna[2], P. Siva kumari

[1]*Asst. professor, Department of Pharmaceutics, Jagan's College of Pharmacy, Jangala kandriga, SPSR Nellore, A.P, India.*
[2]*Jagan's College of Pharmacy, Jangala kandriga, SPSR Nellore, A.P, India*

A B S T R A C T

The valsartan microballoons were prepared by using PVPk30 as a stabilizer & HPMC is a carrier with specific ratio of solvents (Acetone & water). The results were obtained from *in vitro* dissolution data revealed that the prepared valsartan microballoons (F2) were having good buoyancy and entrapment efficiency. It was further concluded that with the variation in concentration of polymer, microballoons of different size, % practical yield and drug content can be obtained with satisfactory results. Microballoons were prepared by using solvent evaporation method, F2 is optimized formulation & it showed highest percentage drug release. SEM results were also showed compared to pure drug the F2 consists of round shaped less particle size (25µm). So, it can be concluded that microballoon drug delivery system can be used as gastro retentive drug delivery system and the mentioned technique is a promising tool for effective microballoons formation.

Keywords: Microballoons, valsartan, solvent evaporation method & gastro retention

A R T I C L E I N F O

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***Corresponding Author**
Gowramma A
Balaji College of Pharmacy,
Ananthapuramu, Andhra Pradesh, India
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1. Introduction

Hollow microspheres (microballoons) are in strict sense, spherical empty particles without core. Microballoons (MB), a multiple unit dosage forms holding a spherical cavity surrounded by a hard polymer shell has been develop as a dosage form illustrate by excellent buoyancy in the stomach. The ultimate goal of any drug delivery system is effective disease/disorder management, minimum side effects and greater patience compliance in the cost effective manner. Microballoons can encapsulate many types of drugs including small molecules, proteins, and nucleic acids

and are easily administered through a syringe needle. They are small spherical particles, with diameters in the micrometer range. Microballoons are sometimes referred to as micro particles. Microballoons can encapsulate many types of drugs including small molecules, proteins, and nucleic acids and are easily administered through a syringe needle.

1.1 Need For Gastro Retention:

- Drugs that are absorbed from the proximal part of the gastrointestinal tract (GIT).
- Drugs that are less soluble or that degrade by the alkaline pH they engage at the lower part of GIT and drugs that are absorbed due to variable gastric emptying time.
- Local or sustained drug delivery to the stomach and proximal Small intestine to treat certain conditions. [Rakhi negia]

1.2 GI Tract Physiology:

The stomach is divided into 3 regions anatomically, fundus, body, and antrum pylorus. The proximal part is the fundus and the body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and acts as a pump for gastric emptying by propelling actions.

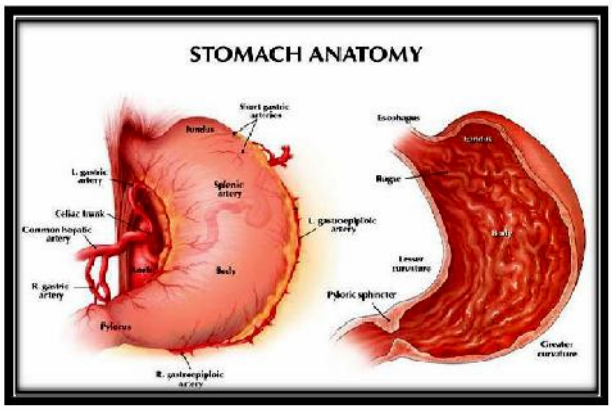

Fig No: 1 Anatomy of Stomach

Gastric emptying occurs during fasting as well as fed states but the pattern of motility is distinct in the 2 states. During the fasting state an interdigestive series of electrical events take place, which cycle through both stomach and intestine every 2 to 3 hours. This is called the interdigestive myloelectric cycle or migrating myloelectric cycle (MMC). [Nemati.H]

1.3 Approaches of gastric retention:

Various approaches have been pursued to increase the retention of an oral dosage form in the stomach. These systems include: [Nilesh Gorde]

- Floating systems
- Bio adhesive systems
- Raft forming systems
- Swelling and expanding systems
- Super porous Hydrogels
- Magnetic systems
- High density systems

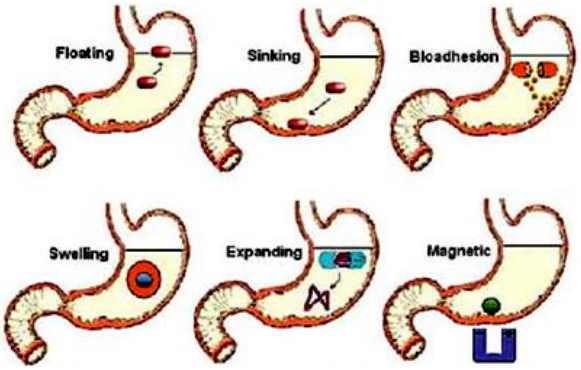

Fig No: 2 working representation of various approaches of GRDDS

1.4 Mechanism of floating systems:

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include introducing floating dosage forms (gas-generating systems and swelling or expanding systems), mucoadhesive systems, high-density systems, modified shape systems, gastric emptying delaying devices and co-administration of gastric emptying delaying drugs. Among these, the floating dosage forms are the most commonly used. Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is eliminated from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration. [N. Bhanu Priya]

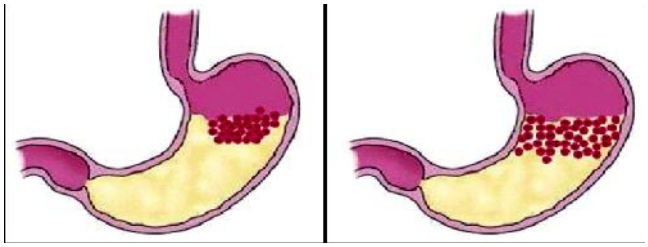

Fig No: 3 Mechanism of floating system

2. Materials and Methods

2.1 Preparation of calibration curve of Valsartan:

100 mg of valsartan was accurately weighed and transferred into 100ml standard flask and then volume was made up of 100ml with ethanol namely called as primary stock solution and from this takes 1ml of solution and dilute with 10ml of ethanol called as secondary stock solution. From the secondary stock solution, Pipette out 0.2ml, 0.4ml, 0.6ml, 0.8ml and 1ml transferred in to the 10ml standard flask and diluted to 10ml with phosphate buffer of pH 7. Absorbance of the prepared solutions was determined spectro-photometrically at 290 nm.

2.2 Preparation of Microballoons:

- **Solvent evaporation method:**

Accurately weighed amount of drug and polymer was mixed with 20 ml of acetone in a beaker. The solution was stirred for 10 minutes. This solution was poured drop wise drop to 0.5% w/v of PVA solution. Add 0.5 % Tween 40 to the solution. The resultant solution was kept under a mechanical stirrer at a constant speed of 400 rpm for 2 hours. The micro balloons were formed and they can be washed, filtered through what man filter paper, collected and dried in hot air oven at 60^0C. [Rakhi negi]

Table 1: Composition of Different Formulations of Microballoons

S. No	Ingredients	F_1	F_2	F_3
1.	valsartan	1.6g	1.6g	1.6g
2.	PVP k30	0.2g	0.2g	0.2g
3.	HPMC	1g	1.5g	2g
4.	Acetone + dichloromethane	20ml	40ml	60ml
5.	Distilled water	20ml	40ml	60ml

Evaluation and characterization of valsartan microballoons:

Percentage practical yield:

Percentage practical yield was calculated to know about percent yield or efficiency of any method and thus its help in selection of appropriate method of formulation. The final weights of the prepared microballons were taken and percentage practical yield was calculated.

$$\% \text{ crystal yield} = \frac{\text{Practical yield}}{\text{Theoritical yield}} \text{ x } 100$$

Buoyancy test:

Accurately weighed 50 mg of microballoons were placed in a beaker containing 100 ml of simulated gastric fluid (SGF) (pH 1.2) and placed in a magnetic stirrer at a speed of 100 rpm.

$$\% \text{ Buoyancy} = \frac{\text{weight of floating microballoons}}{\text{weight of floating+settled microballoons}} X100$$

%Entrapment efficiency:

Entrapment efficiency was determined by taking 20 mg of microballons which were thoroughly triturated and dissolved with 10 ml ethanol in 100ml volumetric flask and volume was made up with 0.1 N Hcl. The resulting solution is then filtered through Whattman filter paper, suitably diluted and the absorbance was measured at 290nm against 0.1N HcI as blank.

$$\%\text{Entrapment efficiency} = \frac{\text{calculated drug concentration}}{\text{Theoritical drug concentration}} X100$$

Drug content:

Equivalent weight of prepared microballoons containing 10 mg of drug were taken and transferred into 100 ml standard flask and volume was made up to 100 ml with ethanol and suitably diluted. The absorbance of the solutions was measured at 290nm.

$$\% \text{ of drug content} = \frac{\text{Observed value}}{\text{Actual value}} X100$$

In vitro dissolution studies:

In vitro dissolution studies were carried by using basket type apparatus. Weighed amount of drug loaded microballoons (equivalent to 100mg of pure drug) were placed in 900ml dissolution medium consists of pH is 1.2 maintained at 37 ± 0.5^0 at 70 rpm. The samples were withdrawn periodically for every 1hr followed by the replacement of an equal volume of the test medium and analysed spectrophotometrically at a range of 290 nm to determine the drug concentration present in the dissolution medium. The initial volume of the dissolution fluid was maintained by adding 5 ml of fresh dissolution fluid after each withdrawal. [Akash Yadav, Mankala SK]

Particle size analysis:

The eye piece micrometer was calibrated by using a standard stage micrometer at 45X. Samples were taken and the suspension was prepared by using propylene glycol and the prepared suspension was mounted on a slide and placed on a mechanical stage. The size of particles was estimated with the help of eye piece micrometer. Around 50 particles were counted to estimate the true mean. [Kawashima Y]

Scanning Electron Microscopy (SEM):

Scanning electron micrographs of valsartan microballons and pure drug powder were taken using a scanning electron microscope (Philips, Philips XL 30 ESEM, and Japan). Samples were fixed on an aluminium stub with conductive double-sided adhesive tape and coated with gold in an argon atmosphere (50 Pa) at 50mA for 50 sec and the results are depicted. [Gupta NV]

Spectroscopic studies:

Standard calibration curve of valsartan:

Table 2: Standard curve data of valsartan using phosphate buffer of pH 7.

S. No	Concentration (µg/ml)	Absorbance
1.	2	0.1711
2.	4	0.3238
3.	6	0.4761
4.	8	0.6341
5.	10	0.8231

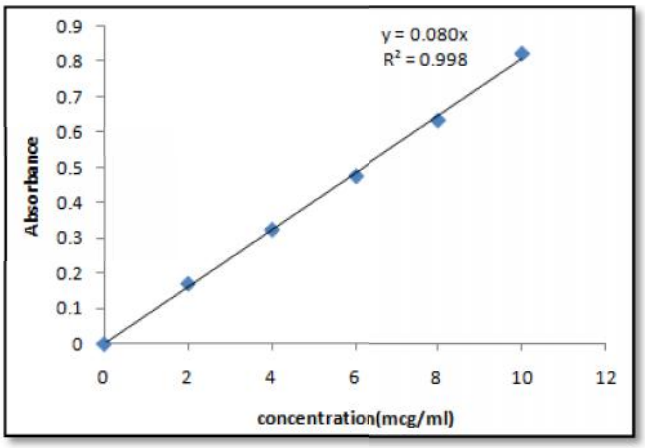

Fig No: 4 Standard plot of valsartan in phosphate buffer of pH 7.4

3. Results and Discussion

Evaluation & characterization of Microballoons:

% Practical Yield:

Table 3: % practical Yield of valsartan microballoons

S. No.	Formulation Code	% Practical yield
1.	F1	88.2%
2.	F2	97.4%
3.	F3	92.1%

% Buoyancy test:

Table 4: % Buoyancy of valsartan microballoons

S. No.	Formulation Code	% buoyancy
1.	F1	67.02
2.	F2	76.32
3.	F3	71.10

%Entrapment Efficiency:

Table 5: %Entrapment Efficiency of valsartan microballoons

S. No.	Formulation Code	% entrapment efficiency
1.	F1	80.11
2.	F2	82.01
3.	F3	79.36

% Drug Content Estimation

Table 6: Drug Content of valsartan Microballoons

S. No.	Formulation Code	% entrapment efficiency
1.	F1	89.01
2.	F2	96.98
3.	F3	92.22

Table 7: Dissolution data of microballoons of valsartan

S. No	Time (min)	% Cumulative Drug Release			
		Pure Drug	F1	F2	F3
1.	15	13.26%	44.26%	59.25%	53.98%
2.	30	26.32%	70.25%	81.25%	75.64%
3.	45	40.03%	79.23%	90.12%	83.54%
4.	60	51.63%	84.3%	98.15%	95.01%

From the results, it was found that the percentage drug release of pure drug was low and only 51.63% was dissolved within 60 minutes. Out of three formulations (F_1-F_3) prepared, F_2 formulation containing PVP k30 as stabilizing agent with HPMC as a carrier i.e., 98.15%. of % drug release. From the results, it was revealed that the F2 showed enhancement in dissolution rate of microballoons occurs due to the presence of Pvp k30 & HPMC. Finally the ratio of polymer: solvent range of F2 is optimized and also it exists highest % drug release.

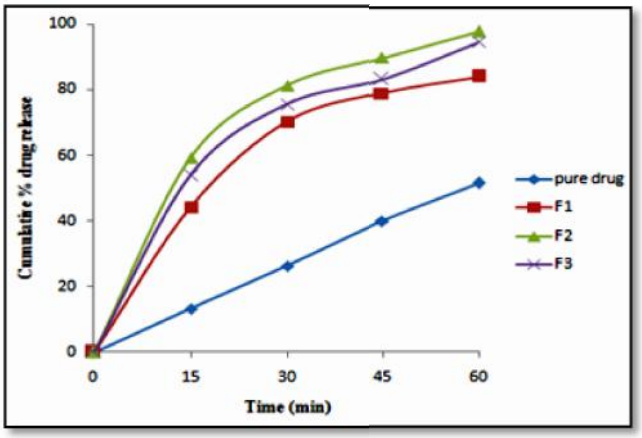

Figure 5: *In vitro* dissolution graph of Valsartan microballoons

Particle size analysis:

Table 8: Mean particle size of valsartan microballoons

S. No.	Formulation Code	Mean particle size (µm)
1.	Pure drug	80.00
2.	F_1	29.63
3.	F_2	24.23
	F_3	27.01

Scanning Electron Microscopy (SEM):

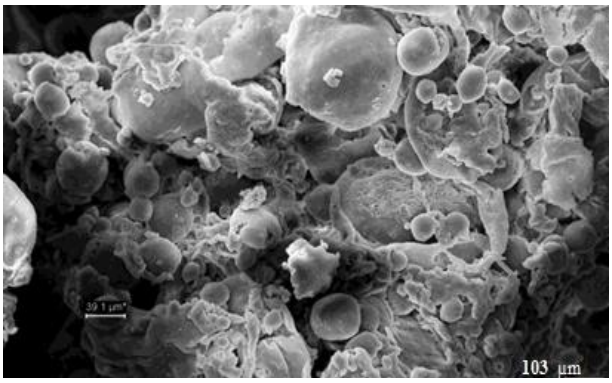

Figure 6: SEM of Pure valsartan

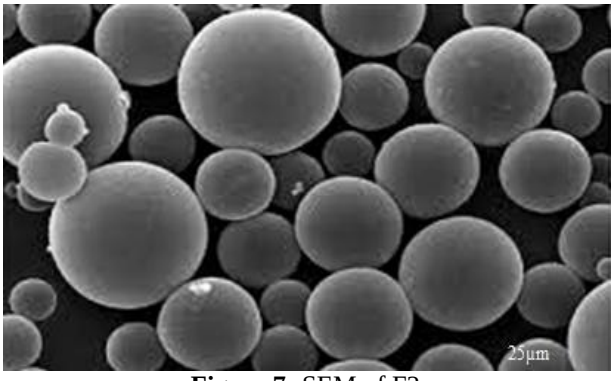

Figure 7: SEM of F2

Scanning electron micrographs of pure valsartan drug powder and valsartan microballoons were shown in above.

Pure valsartan powder showed large shaped crystal habit (103 µm) and F2 showed small round shaped crystals (25 µm).

4. Conclusion

The valsartan microballoons were prepared by using PVPk30 as a stabilizer & HPMC is a carrier with specific ratio of solvents (Acetone & water). The results were obtained from *in vitro* dissolution data revealed that the prepared valsartan microballoons (F2) were having good buoyancy and entrapment efficiency. It was further concluded that with the variation in concentration of polymer, microballoons of different size, % practical yield and drug content can be obtained with satisfactory results. Microballoons were prepared by using solvent evaporation method, F2 is optimized formulation & it showed highest percentage drug release. SEM results were also showed compared to pure drug the F2 consists of round shaped less particle size (25µm). So, it can be concluded that microballoon drug delivery system can be used as gastro retentive drug delivery system and the mentioned technique is a promising tool for effective microballoons formation.

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