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Research

Formulation Development And In-Vitro Evaluations Of Valacyclovir Loaded Mucoadhesive Microspheres

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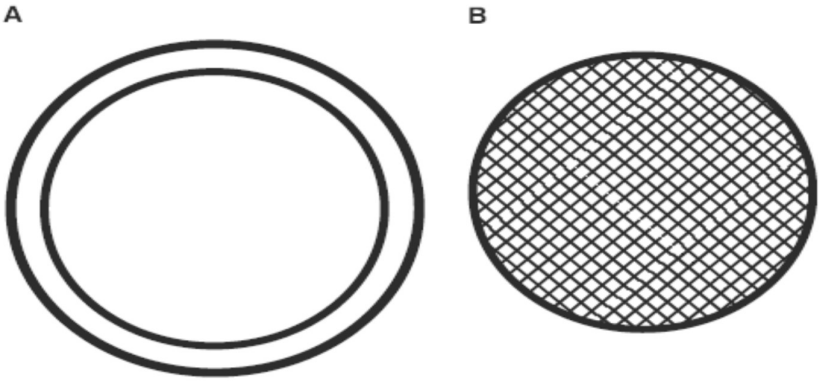
Abstract

In the present work, mucoadhesive microspheres of valacyclovir using Sodium alginate along with Carbopol 934 and HPMC K100 as copolymers were formulated to deliver valacyclovir via oral route.The results of this investigation indicate that Ionotropic gelation method can be successfully employed to fabricate valacyclovir microspheres.FT-IR spectra of the physical mixture revealed that the drug is compatible with the polymers and copolymer used. Micromeritic studies revealed that the avg particle size of the prepared microspheres containing sodium alginate along with carbopol 934 as copolymer had a size range of 625µm to 648µm, and microspheres containing sodium alginate along with HPMC K100 as copolymer had a size range of 548 µm to 612µm. Increase in the polymer concentration led to increase in % Yield, % Drug entrapment efficiency, Particle size. The *invitro* drug release decreased with increase in the polymer and copolymer concentration.The formulation VM3 Sodium alginate along with HPMC K100 showed a maximum release of 85.62 % at 12 hours. Analysis of drug release mechanism showed that the drug release from the formulations followed the best fit higuchi's model of drug release diffusion mechanism and follows zero oreder kinectics. Based on the results of evaluation tests formulation coded VM3 was concluded as best formulation.

Keywords: Mucoadhesive, Microspheres

INTRODUCTION

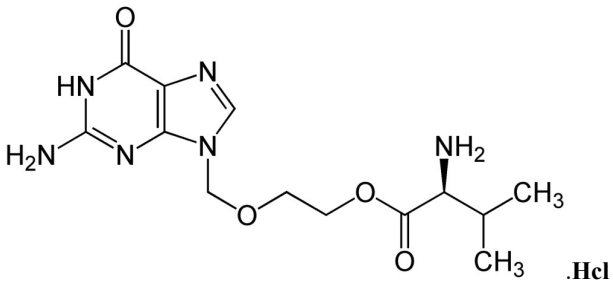
Microspheres can be defined as solid, approximately spherical particles ranging in size from 1 to 1000 µm. They are made of polymeric, waxy, or other protective materials, that is, biodegradable synthetic polymers and modified natural products such as starches, gums, proteins, fats, and waxes. The natural polymers include albumin and gelatin[7.] the synthetic polymers include polylactic acid and polyglycolic acid[1-2]. Two types of microspheres: Microcapsules, where the entrapped substance is completely surrounded by a distinct capsule wall, and micromatrices, where the entrapped substance is dispersed throughout the microsphere matrix.
Microspheres are small and have large surface to volume ratios[3]. At the lower end of their size range they have colloidal properties. The interfacial properties of microspheres are extremely important, often dictating their activity[4].



(A) Microcapsule consisting of an encapsulated core particle and
(B) micromatrix consisting of homogeneous dispersion of active ingredient in particle.

Fig 1: Schematic diagram illustrating microspheres.

DRUG PROFILE

STRUCTURE OF VALACYCLOVIR	
 .**Hcl**	
Chemical data	
Description	white, crystalline powder
Formula	C13H20N6O4HCl.H2O
Molecular Mass	378.8
Melting Point	123.4°c
P^{Ka}	1.90,7.47,9.43
Pharmacokinetic Data	
Protein Binding	13-18 %
V_d	50 L
Half- Life	2.5-3.3 hrs
T_{max} (hours.)	0.75-2.5hrs
C_{max}	3.37 mcg\ml

MATERIALS AND EQUIPMENTS

Materials used

Table 1: Materials used for the formulation development

S.No	MATERIAL	MANUFACTURING COMPANY
1	Valacyclovir	Provided by Chandra labs, Hyderabad
2	Carbopol 940P	SD Fine Chemicals Ltd.,Mumbai
3	HPMC K 100	SD Fine Chemicals Ltd.,Mumbai
4	Sodium alginate	SD Fine Chemicals Ltd.,Mumbai
5	Calcium chloride	SD Fine Chemicals Ltd.,Mumbai

EQUIPMENTS USED

Table 2: Equipments used for the process

S.No.	Name of the Equipment	Manufactured by
1	8 Bowl Dissolution apparatus	Electro Lab
2	22 gauge needle with syringe	Dispovan
3	U.V. Spectrophotometer	Labinda
4	Analytical Balance	Adair Dutt Instruments Pvt. Ltd., AD50B
5	Disintegration apparatus	Electro Lab
6	FTIR	Bruker

METHODOLOGY

Determination of λmax

Stock solution (1000µg/ml) of Valacyclovir was prepared in 0.1N HCL solution. This solution was appropriately diluted with 0.1N HCL to obtain a concentration of 100µg/ ml. The resultant solution was scanned in the range of 200nm to 400nm on UV-Visible spectrophotometer. The drug exhibited a λmax at 255 nm.

Preparation Of Standard Calibration Curve Of Valacyclovir[5]

- 10 mg of Valacyclovir was accurately weighed and dissolved in 10ml of 0.1N HCL buffer (Stock Solution – I) to get a concentration of 1000 µg/ml.
- From the stock solution- I,1ml of aliquots was taken and suitably diluted with 0.1N HCL buffer (Stock Solution-II) to get concentration of 100µg/ml.
- From the stock solution- II,aliquots were taken and suitably diluted with 0.1N HCL to get concentrations in the range of 2 to 10 µg/ml.The absorbance of these samples were analyzed by using UV-Visible Spectrophotometer at 255nm against reference 0.1N HCL.

Fourier Transform Infrared Spectroscopy (Ft-Ir)[6]

In order to check the integrity (Compatibility) of drug in the formulation,FT-IR spectra of the formulations along with the drug and other excipients were obtained and compared using Shimadzu FT-IR 8400 spectrophotometer. In the present study, Potassium bromide(KBr) pellet method was employed. The samples were thoroughly blended with dry powdered potassium bromide crystals. The mixture was compressed to form a disc. The disc was placed in the spectrophotometer and the spectrum was recorded.

Preparation Of Microspheres

Table 3: Composition of different formulations

Formulation code	DRUG: POLYMER Ratio	POLYMER Ratio
VM1	1:1	Sodium Alginate : HPMC K 100 (3:1)
VM2	1:2	Sodium Alginate : HPMC K 100 (3:1)
VM3	1:2.5	Sodium Alginate : HPMC K 100 (3:1)
VM4	1:3	Sodium Alginate : HPMC K 100 (3:1)
VM5	1:1	Sodium Alginate : Carbopol 934 (3:1)

VM6	1:2	Sodium Alginate : Carbopol 934 (3:1)
VM7	1:2.5	Sodium Alginate : Carbopol 934 (3:1)
VM8	1:3	Sodium Alginate : Carbopol 934 (3:1)

RESULTS AND DISCUSSION

Preformulation Studies

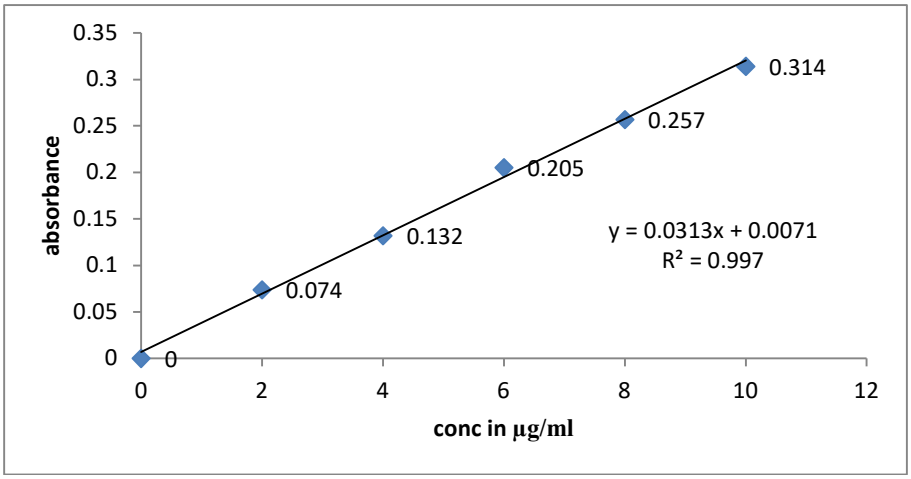


Fig 2: Calibration curve of valacyclovir

Evaluation And Characterisation Of Microspheres

- **Percentage Yield**
- **Drug Entrapment Efficiency**

Table 4: % yield and % drug entrapment efficiency of the prepared microspheres

S.No.	Formulation code	% yield	%Drug entrapment efficiency
1	**VM1**	82.1	77.9
2	**VM2**	85.4	79.3
3	**VM3**	86	85.2
4	**VM4**	88.8	85.6
5	**VM5**	79.9	72.1
6	**VM6**	81.2	78.7
7	**VM7**	84.6	82.3
8	**VM8**	84.9	84.6

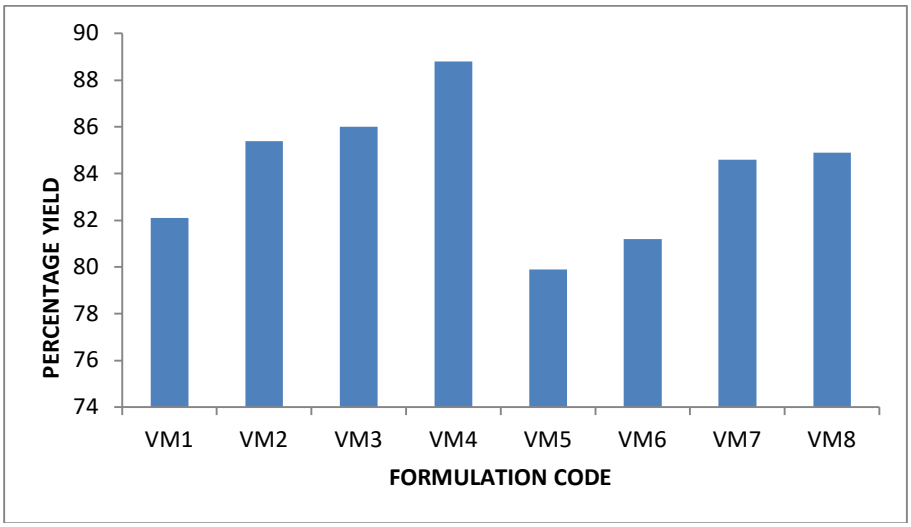


Fig 3: Graphical representation of % yield of formulations VM1 - VM8

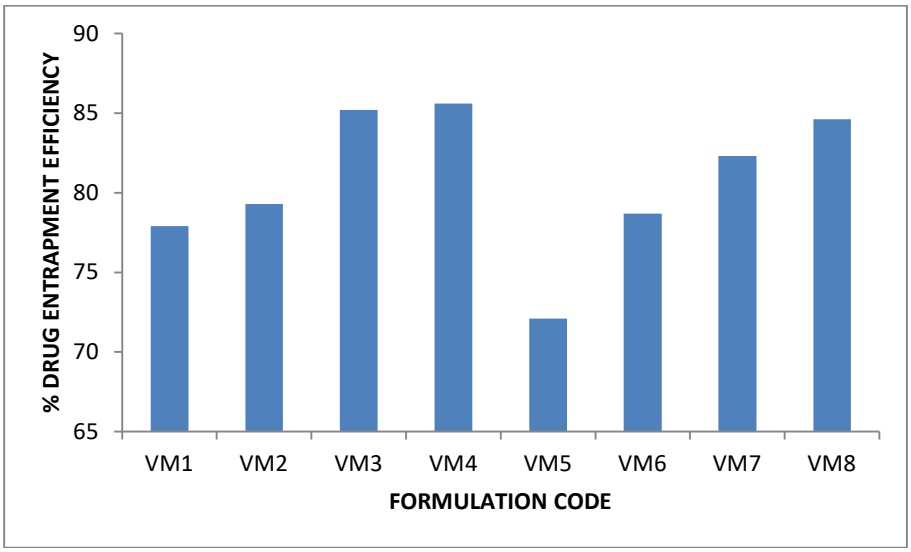


Fig 4: Graphical representation of % drug entrapment efficiency of formulations VM1 - VM8

Particle Size Analysis

Table 5: Average Particle Size analysis for formulation VM1- VM8

Formulation code	Average particle size (µm)
VM1	548
VM2	554
VM3	568
VM4	612
VM5	625
VM6	633
VM7	645
VM8	648

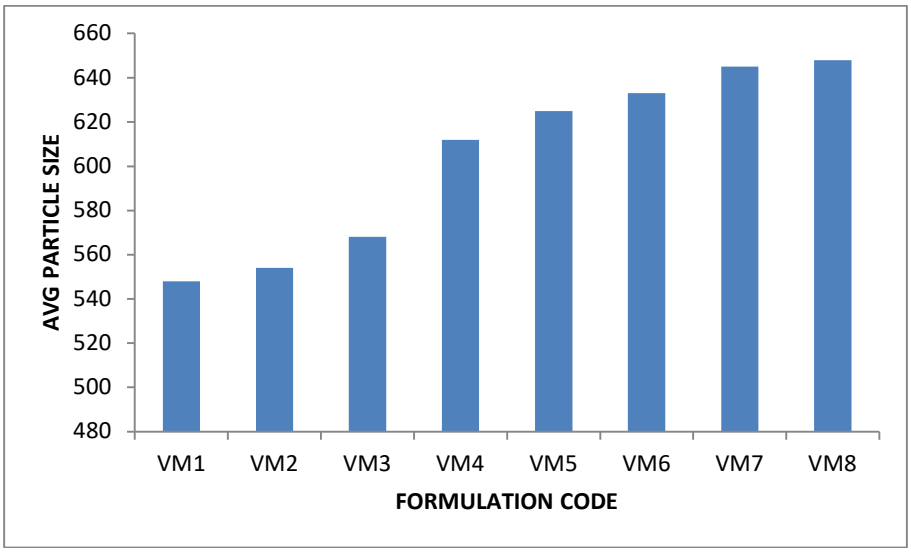


Fig 5: Graphical representation of average particle size for formulations VM1- VM8

In-Vitro Drug Release Studies

Table 6: In-Vitro drug release data of valacyclovir microspheres containing sodium alginate along with HPMC K100 as copolymer.

TIME (hrs)	Cumulative Percent Of Drug Released			
	VM1	VM2	VM3	VM4
0	0	0	0	0
1	15.08	12.60	10.82	10.78
2	29.70	28.01	22.62	21.07
3	32.68	34.80	30.96	28.86
4	39.54	40.68	38.84	34.10
5	44.25	47.13	43.17	45.42
6	51.36	53.69	50.80	56.62
7	72.74	76.82	62.26	67.71
8	80.74	82.31	72.18	70.92
10	--	--	80.11	79.21
12	--	--	85.62	83.40

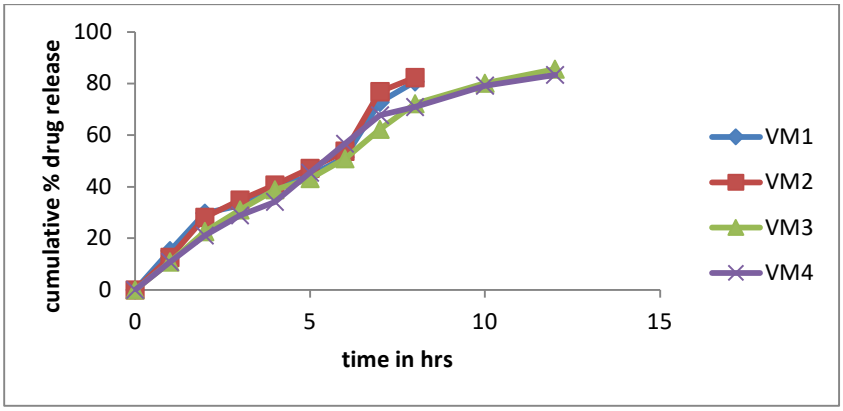


Fig 6: Comparison of In-Vitro drug release profile of valacyclovir microspheres containing sodium alginate along with HPMC K100 as copolymer

Table 7: In-Vitro drug release data of valacyclovir microspheres containing sodium alginate along with Carbopol as copolymer

TIME (hrs)	Cumulative Percent Of Drug Released			
	VM5	VM6	VM7	VM8
0	0	0	0	0
1	9.70	9.61	8.20	8.29
2	15.62	12.07	12.60	11.04
3	22.40	22.46	20.34	18.79
4	36.16	28.60	28.00	26.55
5	43.80	36.90	34.31	36.50
6	50.91	47.22	45.52	43.64
7	55.40	55.07	55.61	54.52
8	61.82	58.09	57.70	58.30
10	68.70	66.58	65.98	62.66
12	75.51	72.80	70.11	64.48

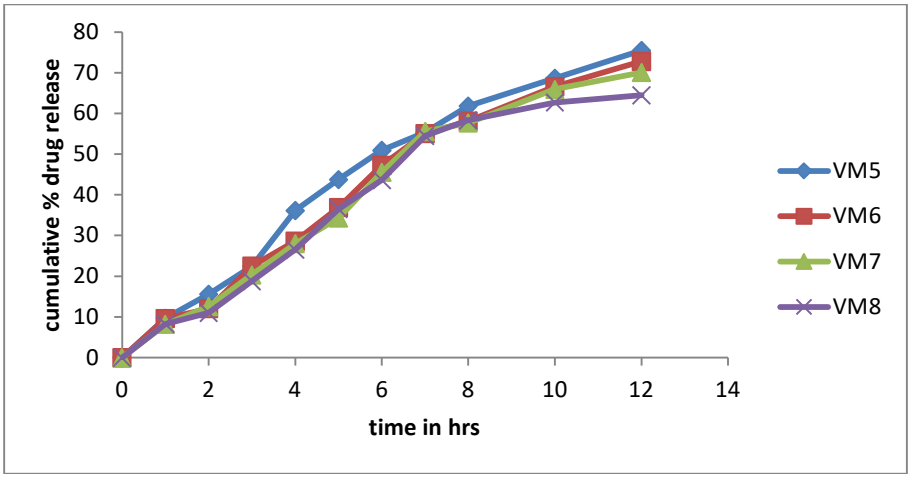


Fig 7:Comparison of In-Vitro drug release profile of valacyclovir microspheres containing sodium alginate along with carbopol 934 as copolymer

SUMMARY AND CONCLUSION

In the present work, mucoadhesive microspheres of valacyclovir using Sodium alginate along with Carbopol 934 and HPMC K100 as copolymers were formulated to deliver valacyclovir via oral route. Details regarding the preparation and evaluation of the formulations have been discussed in the previous chapter. From the study following conclusions could be drawn:

- The results of this investigation indicate that Ionotropic gelation method can be successfully employed to fabricate valacyclovir microspheres.
- FT-IR spectra of the physical mixture revealed that the drug is compatible with the polymers and copolymer used.
- Micromeritic studies revealed that the avg particle size of the prepared microspheres containing sodium alginate along with carbopol 934 as copolymer had a size range of 625µm to 648µm, and microspheres containing sodium alginate along with HPMC K100 as copolymer had a size range of 548µm to 612µm.
- Increase in the polymer concentration led to increase in % Yield, % Drug entrapment efficiency, Particle size.
- The *invitro* drug release decreased with increase in the polymer and copolymer concentration.
- The formulation VM3 Sodium alginate along with HPMC K100 showed a maximum release of 85.62 % at 12 hours.
- Analysis of drug release mechanism showed that the drug release from the formulations followed the best fit higuchi's model of drug release diffusion mechanism and follows zero oreder kinectics.
- Based on the results of evaluation tests formulation coded VM3 was concluded as best formulation.

REFERENCES

1. Mohammed G Ahmed, Satish K BP, Kiran K GB, Formulation and Evaluation of Gastric-Mucoadhesive Drug Delivery Systems of Captopril, JCPR 2010; 2(1): 26-32.
2. PranshuTangri, Mucoadhesive Drug Delivery: Mechanism and Methods of Evaluation, ISSN, 2011; 2 (1); 458-457.
3. Hannah B, Novel bioadhesive formulation in drug delivery, The drug delivery companies report. (2004). 16-19.
4. Mathiowitz E, Chickering DE, Jacob JS (2001) US Pat. No 6,1997, 346.
5. PermenderRathee et al. Gastrointestinal mucoadhesive drug delivery system: A review. Journal of Pharmacy Research 2011, 4(5), 1448-1453.
6. Jasti B., Li X., Cleary G, Recent advances in mucoadhesive drug delivery systems. Polymers, 2003, 194-196.
7. Andrews G.P., Laverty T.P., Jones D.S, Mucoadhesive Polymeric Platforms for Controlled Drug Delivery. Euro. J. Pharm. Biopharm., 71(3), 2009, 505-18.