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EVALUATION AND STABILITY STUDIES OF FORMULATED NORFLOXACIN SUSPENSION

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ABSTRACT

Norfloxacin(1-ethyl-6-fluoro-1,4-dihydro-4-oxo-7-(piperazinyl)-3- uinolinecarboxylic acid).Is a common fluoroquinolones antibacterial drug having the bitter taste . An attempt was made to formulate a suspension of norfloxacin using different suspending agent like, scmc, pvp, papaya pulp powder and a surfactant polysorbate 80. For comparison another suspension of norfloxacin was formulated using the different suspending agents without polysorbate 80. The norfloxacin suspension was formulated using norfloxacin powder, sodium chloride, sodium saccharin, glycerin, paraben concentrate, and purified water. It was found that the product was physically acceptable and the ingredients used in the formula did not affect the chemical stability of the drug under the studied conditions.

Key words: Norfloxacin Suspension, Sodium Chloride, Sodium Saccharin, Glycerin

1. INTRODUCTION

A suspension is a particular class or type of dispersion or dispersed system in which the internal or suspended, phase is dispersed uniformly throughout the external phase, called the suspending medium or vehicle. The internal phase, consisting of a homogeneous or heterogeneous distribution of solid particles having a specific range of sizes, is maintained uniformly in time throughout the suspending vehicle with the aid of a single or a particular combination of suspending agent(s). In addition, unlike a solution, the suspended particles exhibit a minimum degree of solubility in the external phase. When the suspended solids are less than about 1 μm in size, the system is called a colloidal suspension. When the particles are greater than about 1μm the system is called coarse suspension (Gaikwad RV, 2000). The practical upper limit for individual suspendable solid particles in coarse suspensions is approximately 50 to 75 μm. When one or more of the type of solid particles that constitute the internal phase are pharmaceutically useful or physiologically active, the system is known as a pharmaceutical suspension (Aithal KS, 1996) (Sateesh M, 1997).

2. EXPERIMENTAL WORK

2.1 Materials: Norfloxacin was obtained as a gift sample from Dr.Reddy's Labs, Hyderabad, Sorbitol 70% Liquid Lr, Glycerin Lr, Saccharine Sodium Lr was obtained from S.D.Fine-Chem Ltd., Boisar, Propylene Glycol was obtained from Scientific Chemicals, Chennai, and Peppermint Oil Pure Lr was obtained Shreeji Chemicals, Mumbai, and Sunset Yellow Was Obtained from National Chemicals, Vadodara.

2.2 Preparation of Standard Drug Solution: 100 mg of pure Norfloxacin was accurately weighed and transferred to 100 ml volumetric flask, dissolved in acetate buffer pH 4.0, the volume was made upto 100 ml with acetate buffer pH 4.0. From this stock solution, 10 ml was transferred to another 100 ml volumetric flask and the volume was made upto the mark with acetate buffer pH 4.0 to obtain a final volume of 100 μg/ml (Shrishailappa B, 1995) (Shrishailappa B, 1989)(Kanna Babu S, 1999).

2.3 Standard Curve: In a series of 10 ml volumetric flask aliquots of 0.2, 0.4, 0.6, 0.8, 1.0 to 2.0 ml of standard drug solutions were taken and acetate buffer pH 4.0 was added up to 10 ml. Absorption values were measured at 278 nm against a reagent blank.

2.4 Preparation of Norfloxacin Suspension: Prepare peppermint spirit, syrup and finely powder Norfloxacin and suspending agent (SCMC or papaya pulp powder or PVP). Clean the mortar, pestle and other apparatus. Weigh and measure all the ingredients needed for suspension preparation. Take norfloxacin in a mortar and levigated with a solution of wetting agent. Add suspending agent (Scmc/papaya pulp powder/ PVP) into the mortar triturate well. Add glycerin into mortar and triturate the mixture to form a smooth paste. Dissolve saccharin sodium in required purified water, add to step (6) followed by sorbitol, propylene glycol and half of the quantity of syrup. Triturate until a homogeneous mixture is obtained. Add peppermint spirit and colour (sunset yellow FCF) (Chowdary KPR, 1992). Stir the suspension by using a

stirrer at a constant speed to get a homogeneous mixture. Transfer the suspension to the measuring cylinder and make up to final volume with syrup. Finally transfer the suspension to amber color bottle. Label and store in a cool and dry place.

2.5 Evaluation and stability studies of formulated suspension

2.5.1 Dissolution studies of Norfloxacin Suspension: The medium used was 750 ml of acetate buffer pH 4.0. The paddle speed was maintained at 50 rpm and after 5, 10, 15, 20 and 30 minutes 1 ml of sample was withdrawn, diluted to 10 ml with acetate buffer pH 4.0 and absorbance measured at 278 nm. After each withdrawal it was replaced with acetate buffer pH 4.0. The percentage of drug release was calculated (Cary EJ, 2001)

3. RESULTS AND DISCUSSION

An attempt was made to formulate a suspension of norfloxacin using different suspending agent like, scmc, pvp, papaya pulp powder and a surfactant polysorbate 80. For comparison another suspension of norfloxacin was formulated using the different suspending agents without polysorbate 80. All the formulation was subjected for evaluation and stability studies. Observing the results obtained from dissolution studies it was found that at zero time, formulation containing scmc as a suspending agent exhibited a steady state release and maximum concentration of 83% was released at 20 minutes and formulation containing papaya pulp powder, pvp released a maximum concentration of 80% and 79% at 20 minutes respectively. Dissolution studies carried out at zero time, in the formulation of norfloxacin suspension without polysorbate 80 using scmc as a suspending agent exhibited a steady state maximum release of 78.5% (SCMC) and papaya pulp powder, pvp exhibit a maximum concentration release of 74.5% and 73.7% at 20 minutes respectively(Table 4). The formulation containing polysorbate 80 exhibited better release than the formulation without it.Dissolution studies were further carried out after 1.5, 3.0, and 6.0 months respectively at room temperature and 40^{o}C, to observe the stability of the formulated suspension. The results obtained from these studies revealed that at higher temperature also that is 40^{o}C, the suspension were stable. Studies on content uniformity were carried out for the formulations containing surfactant (polysorbate 80) at zero time and after 1.5, 3.0, 6.0 months respectively. The results showed that the percentage of drug concentration was almost similar in all the formulations at room temperature and 40^{o}C. Regarding sedimentation volume it was observed that the formulations containing scmc as a suspending agent with polysorbate 80 showed a high volume of sedimentation, followed by papaya and PVP. In all the formulation redispersibility was comparatively easy and uniform. The particle size distribution in formulated suspension containing suspending agent SCMC, papaya pulp powder and pvp with polysorbate 80 was in the range of 15-25µm. The pH of all the formulation at all time intervals and at elevated temperature of 40^{o}C was found to be the same and no change in pH 6-8 was observed. There was no appreciable change in colour and odour for all the formulations during the entire course of the study.

3.1 Assay of Norfloxacin suspension: The suspension containing an amount equivalent to 100 mg of Norfloxacin was transferred to a 100 ml volumetric flask. To this acetate buffer pH 4.0 was added and made upto volume. Shake the contents and filter. 10 ml of filtrate was further diluted to 100 ml with acetate buffer pH 4.0. Finally 1 ml of this is taken in a 10 ml volumetric flask made up to the volume with acetate buffer pH 4.0 to obtain a final concentration of 10 µg/ml. The final volume was measured at 278 nm against acetate buffer pH 4.0 as blank.

3.2 Sedimentation volume: 100 ml of each of the formulations were stored in stoppered measuring cylinders at room temperature and at 40^{o} C. the height of sedimentation was recorded to calculate the sedimentation volume.

3.3 Sedimentation redispersibility: After the sedimentation studies, the cylinders were rolled on a horizontal surface at the rate of 10-15 revolutions per minute. The ease of redispersibility was judged comparatively.

3.4 pH change: The change in pH in the formulation was studied using systronic digital pH meter.

3.5 Particle size measurement: Size of Norfloxacin particles in the suspensions were measured by microscopy. The range of particle size was estimated.

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Table 1 Formulation table of Norfloxacin suspension

Ingredient	Quantity
Norfloxacin	20 mg/ml
SCMC/ Papaya pulp powder/PVP	0.1 %
Saccharin Sodium	0.1 %
Sorbitol solution	10 %
Glycerol	10 %
Propylene glycol	20%
Peppermint spirit BP	3 %
Purified Water	30 %
Syrup BP to	100ml

Table 2 Standard graph of Norfloxacin

S.No	Concentration in µg/ml	Absorbance at 278 nm
1	2	0.2513
2	4	0.4910
3	6	0.7411
4	8	0.9929
5	10	1.2381

Table 3 Dissolution studies at zero time Suspension containing Polysorbate 80

Time in minutes	% of Drug Released		
	SCMC	PVP	Papaya
5	21.7	15.7	18.7
10	37.5	31.5	35.2
15	55.5	51.0	53.2
20	83.2	79.5	80.2
30	78.0	72.7	74.2

Table 4 Dissolution Studies at zero time Suspension not containing Polysorbate 80

Time in minutes	% of Drug Released		
	SCMC	PVP	Papaya
5	18.0	13.5	15.7
10	34.5	28.5	32.2
15	50.2	48.5	49.4
20	78.5	73.7	74.2
30	74.2	68.2	70.5

Table 4 Dissolution studies after 1.5 months

Time in Time of minutes	% of Drug Released					
	SCMC		PVP		Papaya	
	RT	40°C	RT	40° C	RT	40° C
5	20.2	21.0	14.2	15.0	17.2	18.0
10	36.0	36.7	29.2	30.0	33.7	34.5
15	54.0	54.7	49.5	50.2	51.7	52.5
20	81.7	82.5	75.7	77.2	77.2	78.7
30	76.5	77.2	70.5	72.0	72.7	73.5

Table 5 Dissolution studies after 3 months

Time in minutes	% of Drug Released					
	SCMC		PVP		Papaya	
	RT	40° C	RT	40° C	RT	40° C
5	19.5	20.2	13.5	14.2	16.5	17.2
10	35.2	36.0	28.5	29.2	33.0	33.7
15	53.2	54.0	48.7	49.5	51.0	51.7
20	81.0	81.0	75.0	76.5	76.5	77.2
30	75.7	75.7	69.7	71.2	72.0	72.7

Table 6 Dissolution studies after 6 months

Time in minutes	% of Drug Released					
	SCMC		PVP		Papaya	
	RT	40° C	RT	40° C	RT	40° C
5	18.7	19.5	12.7	13.5	15.7	16.5
10	33.7	34.5	27.7	28.5	32.2	33.0
15	52.5	53.2	48.7	48.7	50.2	51.0
20	79.5	80.2	75.7	75.7	75.7	76.5
30	75.0	75.0	70.5	70.5	71.2	72.0

Table 7 Table Stability studies for different

Time in months	% of Drug Concentration					
	SCMC		PVP		Papaya	
	RT	40° C	RT	40° C	RT	40° C
0	99.87	99.87	99.16	99.16	99.81	99.81
1.5	99.88	99.49	98.88	98.45	98.41	99.03
3.0	98.85	98.45	98.09	97.98	98.73	98.18
6.0	98.02	97.75	97.92	97.1	97.95	97.21

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Table 8 Sedimentation volume

Time in months	Sedimentation volume (H_u/H_o)					
	SCMC		PVP		Papaya	
	RT	40° C	RT	40° C	RT	40° C
0	0.82	0.82	0.65	0.65	0.78	0.78
1.5	0.75	0.71	0.52	0.48	0.61	0.58
3.0	0.61	0.58	0.41	0.38	0.54	0.50
6.0	0.52	0.48	0.38	0.38	0.45	0.43

Figure 1 Dissolution studies at zero time suspension containing Polysorbate 80

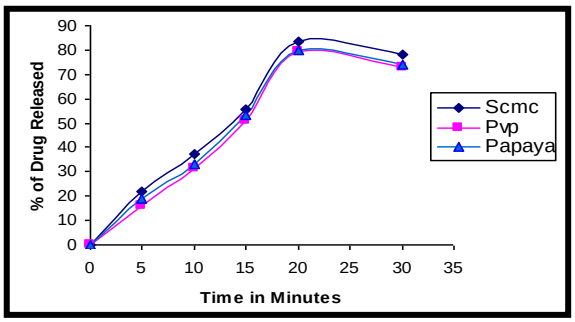

Figure 2 Dissolution studies at the end of 45 days at room temperature

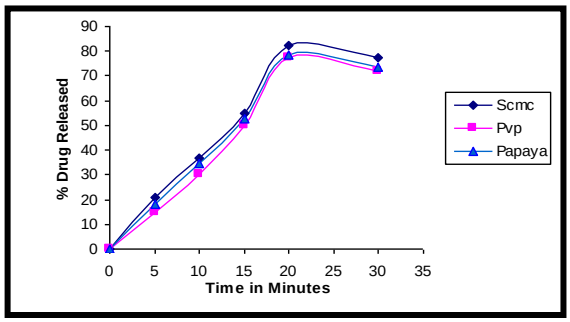

Figure 3 Dissolution studies at the end of 45 days at 40°C

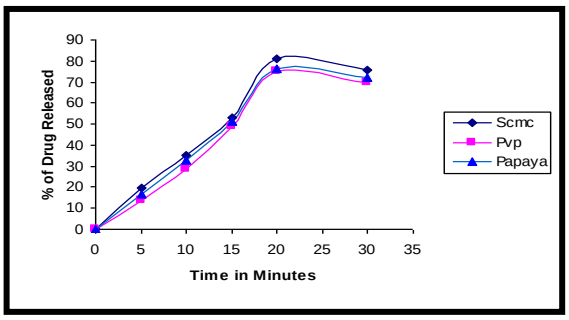

Figure 4 Dissolution studies at the end of 90 days at room temperature

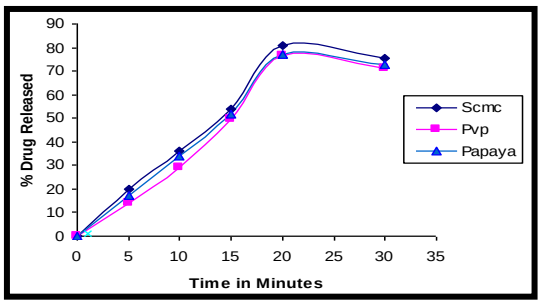

Figure 5 Dissolution studies at the end of 90 days at 40°C

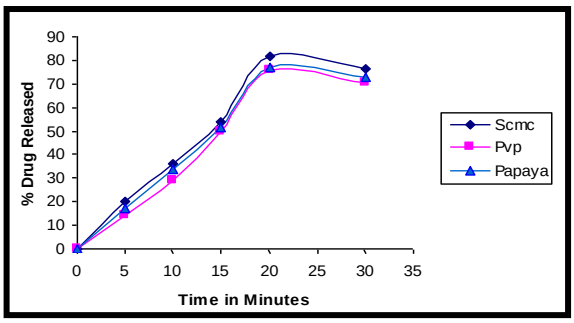

Figure 6 Dissolution studies at the end of 90 days at room temperature

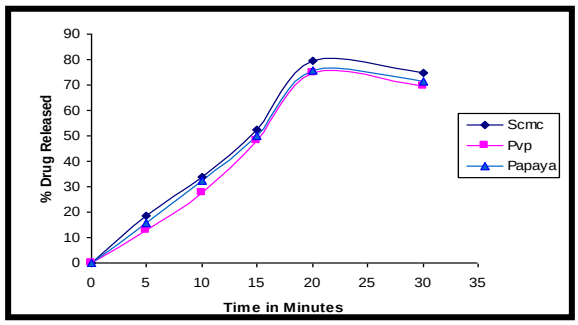

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Figure7 **Dissolution studies at the end of 6 month at 40°C**

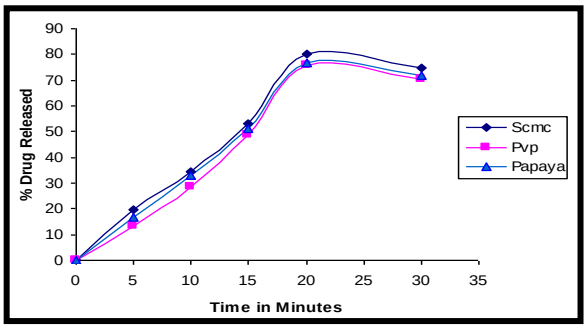


Figure 8 Assay of suspension containing SCMC at room temperature

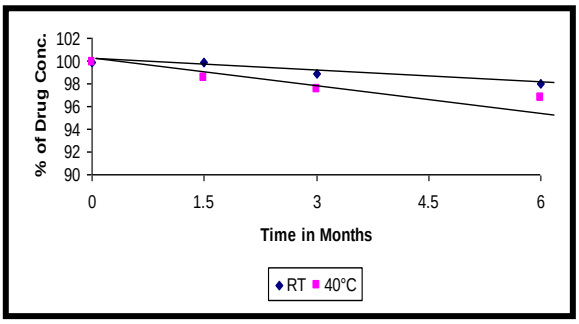


Figure 9 Assay of suspension containing PVP at room temperature

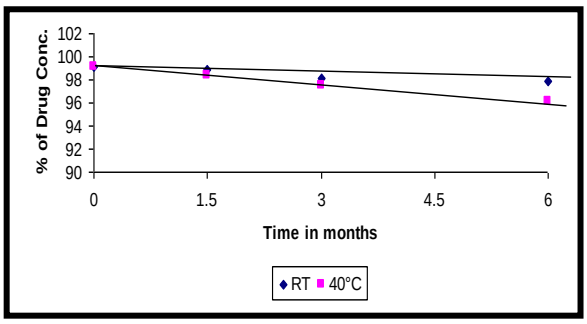
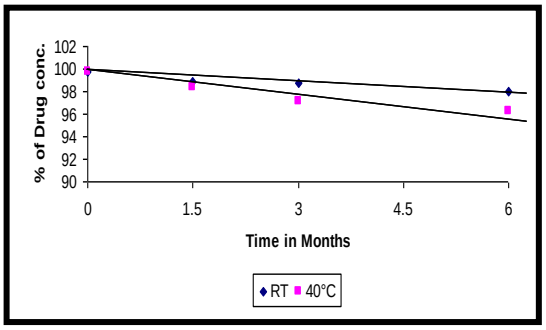


Figure 10 Assay of suspension containing papaya at room temperature



4. CONCLUSION

Based on the results obtained from the dissolution studies, assay, particle size distribution, re-dispersability, pH and stability studies of the formulated suspensions, we could justify the use of papaya pulp powder as a natural suspending agent. The results also reveal that the use of a surfactant polysorbate80 in a concentration of 0.1% in all the formulation has a positive influence on the release characteristics of the drug. To conclude papaya powder could be used as a Natural suspending agent.

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