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FORMULATION AND EVALUATION OF HOLLOW MICROSPHERES OF ACECLOFENAC

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Keywords:

Gastric retention, hollow microspheres, low density

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ABSTRACT

The problem of short gastric residence time encountered with an oral CR formulation. One of the technologies to overcome this problem is formation of floating drug delivery systems. Hollow microspheres represent this type of system. Hollow microspheres loaded with drug in their outer polymer shelf. The problem of short gastric residence time with an oral CR formulation can be overcome with these systems. These systems have a bulk density of <1 as a result of which they can float on the gastric contents. The hollow microspheres of Aceclofenac were formulated using Solvent Evaporation Method. The polymers used were HPMC K4, HPMC K15 and Carbopol. The concentration of polymers showed prominent effect on In vitro release of drug. The combination of HPMC K4 and Carbopol showed more satisfactory gastro retentive property and uniform release than combination of HPMC K15 and Carbopol. In case of combination of HPMC K4 and Carbopol the formulation which had high ratio of Carbopol/ HPMC K4 showed more satisfactory gastro retentive property and uniform release than other formulations. The release of Aceclofenac from the prepared formulations was found to follow Zero order kinetics. This combination also showed excellent flow property. Entrapment efficiency also found better for this combination.

INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug at the proper site in the body and then maintain the desired drug concentration [1]. Conventional drug delivery system maintains the drug concentration within the therapeutically effective range needed for treatment, only when taken several times a day [2]. The high level of patient compliance has been observed in taking oral dosage forms is due to the ease of administration and handling of these forms. Although a lot of advancements have been seen in oral controlled drug delivery system in the last few decades, this system has been of limited success in case of drugs with a poor absorption window throughout the GIT (Gastro Intestinal Tract). To modify the GI transit time is one of the main challenge in the development of oral controlled drug delivery system. [3] Success of oral drug delivery system depends on its degree of absorption through GIT. Thus, the idea of enhancing drug absorption pioneered the idea of development of Gastroretentive drug delivery system (GRDDS) [4]. The ability of gastroretentive systems to remain in the gastric region for a longer period significantly prolong the gastric retention time of drugs. Improved bioavailability, reduction in drug waste and improvement in solubility of drugs that have limited solubility in high pH environment can be achieved by prolonging gastric retention of drugs. [5,6] It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to provide better availability of new products with new therapeutic possibilities and substantial benefits for patients. [7,8] Gastroretentive delivery systems (GRDS), however, are not suitable for drugs that may cause gastric lesions, e.g., non-steroidal anti-inflammatory agents, Drug substances that are unstable in the strong acidic environment of the stomach are not the suitable candidates to be incorporated in such systems. [9] Floating Drug Delivery Systems (FDDS) first described by Davis (1968), are low-density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach for a prolonged period. While the system floats over the gastric contents, the drug is released slowly at the desired rate, which results in increased gastroretention time and reduces fluctuations in plasma drug concentration. Hollow microspheres are gastroretentive drug delivery systems based on non-effervescent approach. They are spherical empty particles without core. They possess the unique advantages of multiple unit systems and their center hollow space imparts good floating properties making them promising buoyant systems. [10]

ADVANTAGES:

Hollow microspheres offer various advantages including:

1. Improved patient compliance and convenience owing to less frequent dosing.
2. Decreased local and systemic side effects by reduction in fluctuation in steady state level.
3. Increased drug utilization by decreased total amount of drug used.
4. Avoid drug accumulation on chronic dosing.
5. Reduction in health care costs through improved therapy and shorter treatment period. [11]
6. Avoidance of gastric irritation due to sustained release effect. [12]

EXPERIMENTAL WORK:

Formula of different batches of Aceclofenac Microballoons:

Formulation	Drug (mg)	HPMC K4 (mg)	HPMC K15 (mg)	Carbopol (mg)	Ethanol : DCM	Temp (°C)
F1	50	50	-	-	1:1	Room Temp.
F2	50	50	-	50	1:1	Room Temp.
F3	50	50	-	75	1:1	Room Temp.
F4	50	-	50	-	1:1	Room Temp.
F5	50	-	50	50	1:1	Room Temp.
F6	50	-	50	75	1:1	Room Temp.

Material and Method used: Solvent Evaporation Method

Aceclofenac was obtained as a gift sample from Sureka pharma, Indore. HPMC K4, HPMC K15 and Carbopol were purchased from Evonik India Pvt. Ltd. Mumbai. All other chemicals and reagents used were of analytical grade.

Preparation of Aceclofenac floating hollow microspheres:

Aceclofenac, HPMC and Carbopol were dissolved in a mixture of ethanol and dichloromethane (DCM) at room temperature. This was poured into 250 mL water containing 0.01% Tween 80 maintained at a temperature of 30–40 °C and subsequently stirred at ranging agitation speed for 20 min to allow the volatile solvent to evaporate. The microspheres formed were filtered, washed with water and dried.

RESULTS:

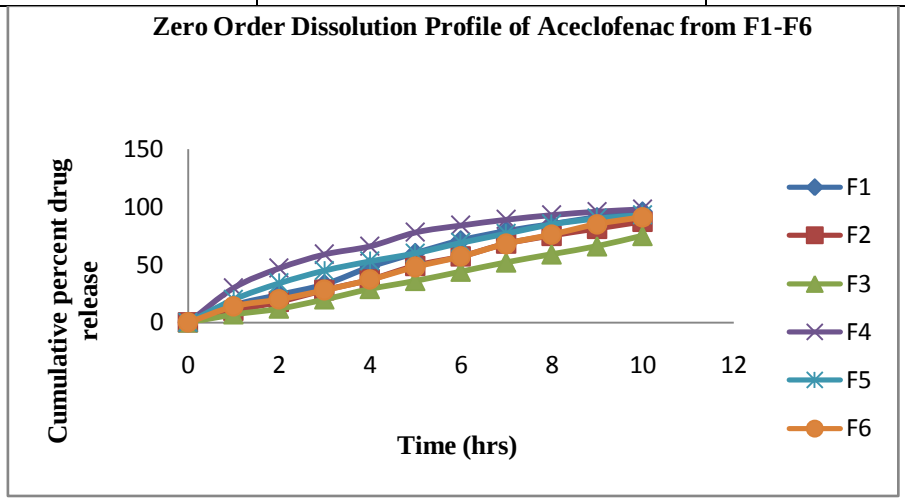
% Buoyancy of microballoons at different time intervals:

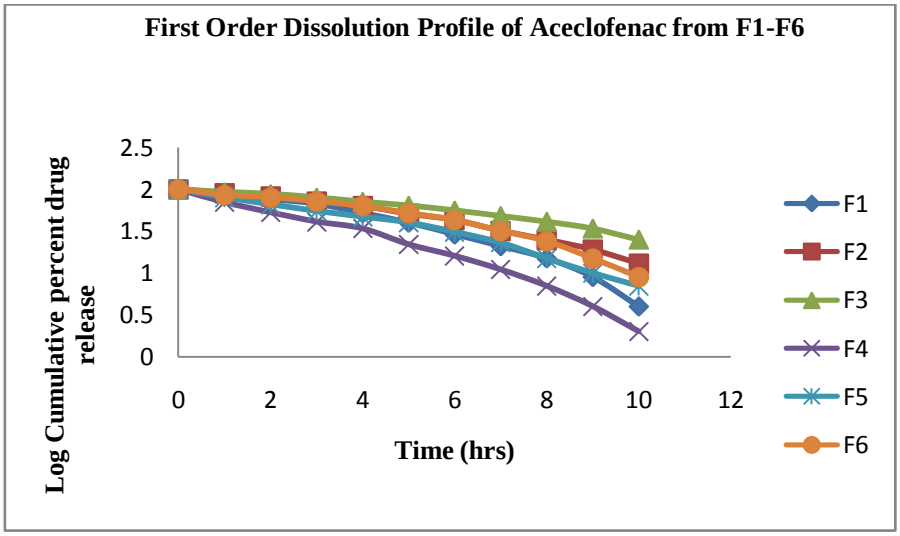
Formulations	Time (hrs)							
	1	2	3	4	5	6	7	8
F1	88.42	89.21	88.21	86.54	85.84	82.61	77.44	76.06
F2	91.33	90.58	87.29	86.64	84.22	81.48	78.19	77.17
F3	94.12	92.41	91.25	88.29	90.34	89.18	86.42	84.31
F4	90.27	89.35	87.49	84.77	83.41	80.82	77.21	74.54
F5	87.59	85.25	84.11	82.46	81.17	78.34	74.28	71.43
F6	85.16	83.37	82.54	80.74	79.56	74.41	71.37	69.62

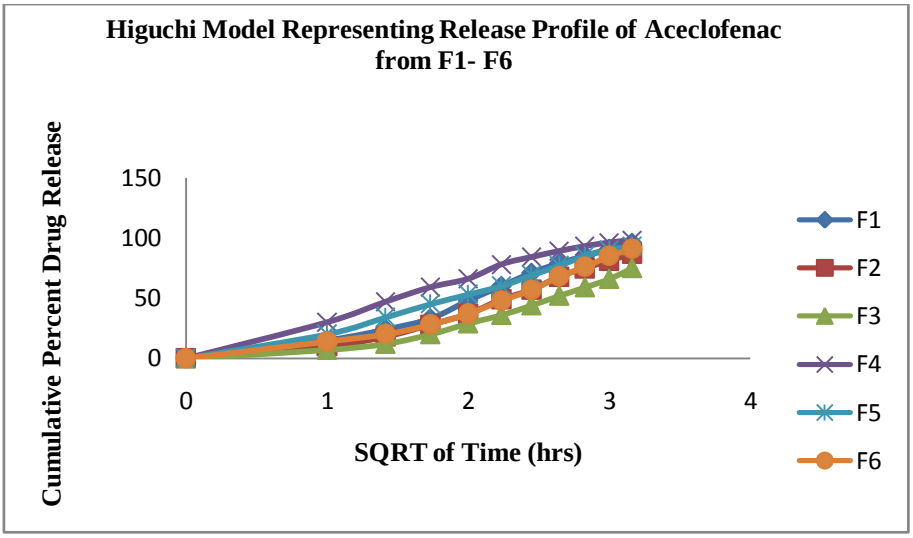
Formulation	Bulk Density (gm/cc)	Tapped Density (gm/cc)	Carr's index	Hausner's Ratio	Angle of repose
F1	0.673	0.776	13.265	1.152	28.41°
F2	0.589	0.666	11.607	1.131	23.57°
F3	0.628	0.702	10.476	1.117	16.78°
F4	0.661	0.758	13.065	1.149	29.73°
F5	0.611	0.717	12.962	1.148	12.78°
F6	0.634	0.634	11.538	1.130	21.32°

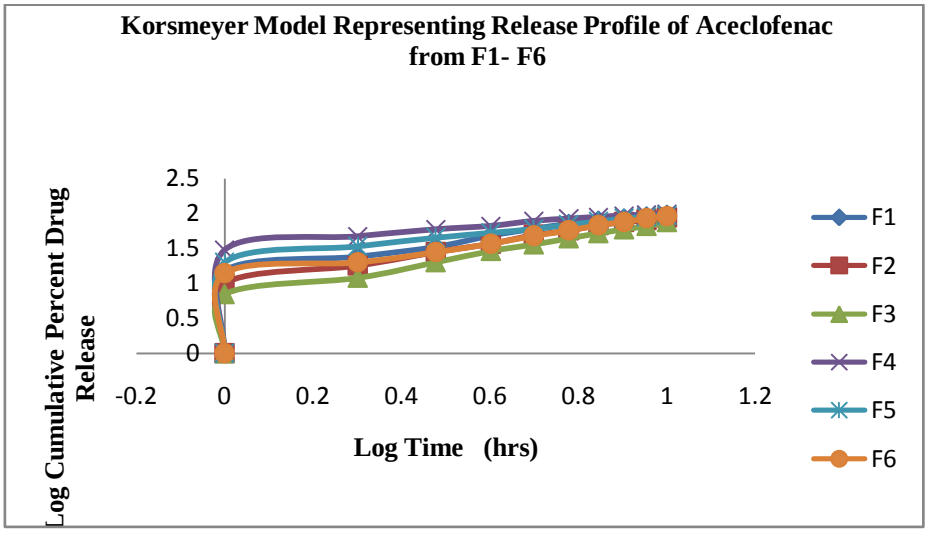
Entrapment efficiency (%) and Percentage Yield

Formulation	Entrapment efficiency (%)	Percentage Yield
F1	74.64	77.63
F2	78.16	74.57
F3	84.59	80.34
F4	72.34	73.69
F5	75.21	70.86
F6	79.25	82.34









Kinetic of invitro release from floating tablet of Aceclofenac

Formulation	Zero Order R^2	First order R^2	Higuchi plot R^2	Korsmeyer plot R^2
F1	0.980	0.932	0.950	0.745
F2	0.994	0.960	0.930	0.809
F3	0.998	0.957	0.903	0.863
F4	0.882	0.974	0.990	0.566
F5	0.963	0.965	0.986	0.655
F6	0.997	0.919	0.924	0.762

DISCUSSION

- Floating hollow microspheres of Aceclofenac were prepared by the Solvent Evaporation Method using different combination of HPMC K4, HPMC K15 and Carbopol with a view to obtain gastroretentive sustain release for oral drug delivery.
- In vitro Drug release studies: % drug release from formulation F1, F2, F3 shows that when concentration of polymers increase % drug release also increased. But the time for

drug release is more for F3 as compare to F1 and F2. It indicates that F3 has more sustain release effect than F2 and F3. Similar results also obtained for formulations F4, F5, F6. F6 had more sustained release effect than F4 and F5. But when we compared F3 and F4 it was found that F4 showed burst release initially while F3 showed uniform release during the whole period. F3 also showed long period for drug release as F6. It indicates that when we increase the ratio of Carbopol and HPMC the drug release time also increased. In HPMC, HPMC K15 showed burst release while HPMC K4 showed uniform release. All these results indicate that the formulation F3 is best formulation than F1, F2, F4, F5 and F6.

- The Buoyancy was determined. The % Buoyancy of formulations F1, F2, F3, F4, F5, F6 after 8 hours were obtained as76.06, 77.17, 84.31, 74.54, 71.43 and 69.62 respectively. It was found that F3 showed more floating time than other formulations. It indicates that F3 showed best gastro retentive property than F1, F2, F4, F5 and F6.
- The Entrapment efficiency (%) of formulations F1, F2, F3, F4, F5, F6 were obtained as 74.64, 78.16, 84.59, 72.34, 75.21 and 79.25 respectively.
- The Percentage Yield of formulations F1, F2, F3, F4, F5, F6 were obtained as 77.63, 74.57, 80.34, 73.69, 70.86 and 82.34 respectively.

CONCLUSION AND SUMMARY:

The hollow microspheres of Aceclofenac were formulated using Solvent Evaporation Method. The polymers used were HPMC K4M, HPMC K15M and Carbopol 934P. The concentration of polymers showed prominent effect on In vitro release of drug. The R^2 value of Zero order fits to the R^2 value of Higuchi. It indicates that the drug release from the hollow microsphere follow zero order kinetics. The combination of HPMC K4M and Carbopol 934P showed more satisfactory gastro retentive property and uniform release than combination of HPMC K15M and Carbopol 934P. In case of combination of HPMC K4M and Carbopol 934P the formulation which had high ratio of Carbopol 934P / HPMC K4 showed more satisfactory gastro retentive property and uniform release than other formulations. The release of Aceclofenac from the prepared formulations was found to follow Zero order kinetics. This combination also showed excellent flow property. Entrapment efficiency also found better for this combination.

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