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FORMULATION DEVELOPMENT AND *IN-VITRO* EVALUATION OF DOCETAXELLOADED FLOATING MICROSPHERES

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ABSTRACT

The present study has been a satisfactory attempt to formulate floating microspheres of Docetaxel, a new anti-mitotic chemotherapy medication used mainly for the treatment of breast, ovarian and non-small cell lung cancer. From the experimental results it can be concluded that,FT-IR study shows no significant shifting of the peaks therefore it confirms the short term stability of the drug in the beads. Biocompatible polymers like can be chitosan and albumin used to formulate microspheres. Good percentage drug entrapment and practical yields were obtained with both the polymers. Theflowpropertiesofallformulationswerewithintheacceptablerangeand therefore they could be easily filled into capsules. Cumulative percentage drug release significantly decreased within creasein polymer concentration. The overall curve fitting in to various mathematical models was found to be on anaverage. The formulations D7 best fitted in to first order kinetic model and Higuchi model. Thus, the formulated microspheres seem to be a potential candidateas an oral controlled drug delivery system in prolonging the drug release and increasing the bioavailability of drug.

Key Words: floating microspheres, Docetaxel

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INTRODUCTION

For many decades, medication of an acute disease or a chronic disease has been accomplished by delivering drugs to the patients via various pharmaceutical dosage forms like tablets, capsules, pills, creams, ointments, liquids, aerosols, injectables and suppositories as carriers. To achieve and then to maintain the concentration of drug administered within the therapeutically effective range needed for medication, it is often necessary to take this type of drug delivery systems several times in a day. This results in a fluctuated drug level and consequently undesirable toxicity and poor efficiency. This factor as well as other factors such as repetitive dosing and unpredictable absorption leads to the concept of controlled drug delivery systems. The word new or novel in the relation to drug delivery system is a search for something out of necessity. An appropriately designed sustained or controlled release drug delivery system can be major advance toward solving the problem associated with the existing drug delivery system. Oral controlled release dosage forms have been developed over the past three decades due to their considerable therapeutic advantages such as ease of administration, patient compliance and

flexibility in formulation. However, this approach is be dilled with several physiological difficulties such as inability to restrain and locate the controlled drug delivery system within the desired region of the gastrointestinal tract (GIT) due to variable motility and relatively brief gastric emptying time (GET) in humans which normally averages 2-3 hr through the major absorption zone, i.e., stomach and upper part of the intestine can result in incomplete drug release from the drug delivery system leading to reduced efficacy of the administered dose. The objective in designing a controlled release system is to deliver the drug at a rate necessary to achieve and maintain a constant drug blood level. This rate should be similar to that achieved by continuous intravenous infusion where a drug is provided to the patient at a rate just equal to its rate of elimination. This implies that the rate of delivery must be independent of the amount of drug remaining in the dosage form and constant over time, i.e release from the dosage form should follow zero-order kinetics (1-4).

Aim of the study is to formulate Docetaxel microspheres using different polymers by heat stabilization method.

MATERIALS AND METHODS

Heat stabilization technique (5-7)

80mg of Drug is dispersed in mixture of 5ml of 1%w/v albumin solution, 5ml of 2%w/v chitosan in 2% acetic acid and pour into 5ml of 15% w/v gelatin solution (water) containing 1.5% w/v $CaCO_3$ and syringe in to 25ml of Glutaraldehyde containing 20ml Tween 80 1ml gently stirred for 10min at 60-70^{0}c and 1000rpm (w/o emulsion is formed) then it is cooled at 50 ^{0}c for 30min , washed with petroleum ether and dried at 45^0 c (Table-1).

Table-1 Prepared formulation of Floating Beads

S.No.	FORMULATION CODE	DRUG:POLYMER RATIO	POLYMER RATIO (ALBUMIN: CHITOSAN)
1	**D_1**	**1:1**	**1:1**
2	**D_2**	**1:1.5**	**1:2**
3	**D_3**	**1:2**	**1:3**
4	**D_4**	**1:1.5**	**2:1**
5	**D_5**	**1:2**	**1:1**
6	**D_6**	**1:2.5**	**2:3**
7	**D_7**	**1:2**	**3:1**
8	**D_8**	**1:2.5**	**3:2**
9	**D_9**	**1:3**	**1:1**

In vitro drug release study

The dissolution studies were performed in a fully calibrated eight station dissolution test apparatus (37 ± 0.5^{0}C, 100 rpm) using the USP type – I rotating basket method in 0.1N HCl (900ml). A quantity of accurately weighed microspheres equivalent to 80 mg Docetaxeleach formulation was employed in all dissolution studies. Aliquots of sample were withdrawn at predetermined intervals of time and analyzed for drug release by measuring the absorbance at the same time the volume withdrawn at each time intervals were replenished immediately with the same volume of fresh pre-warmed 0.1N HCl maintaining sink conditions throughout the experiment.

RESULTS AND DISCUSSION

All the formulations were evaluated for bulk density, tapped density, % compressibility, hausner's ratio and angle of repose. The results of % compressibility, hausner's ratio and angle of repose were found to be <16, <1.25 and <30 respectively. These results show that the formulations have excellent flow properties (Table-1).

Table-1 Data for Docetaxel Microspheres for micro particle analysis

Formulation code	Bulk density (g/cc)	Tapped density (g/cc)	Carr's Index	Hausner Ratio	Angle of repose(θ)
D1	0.42±0.045	0.50 ± 0.09	16.01±0.1	1.19±0.02	28.06± 0.31
D2	0.46±0.045	0.52 ± 0.07	11.53±0.6	1.13±0.04	27.58± 0.15
D3	0.44±0.038	0.50 ± 0.09	12.00±0.8	1.14±0.08	28.44± 0.11
D4	0.44±0.045	0.51 ± 0.04	13.72±0.1	1.15±0.06	28.36± 0.13
D5	0.43±0.044	0.51± 0.01	15.68±0.6	1.18±0.08	28.52± 0.19
D6	0.45±0.044	0.52 ± 0.04	13.46±0.8	1.15±0.09	29.32± 0.19
D7	0.50±0.046	0.57 ± 0.04	12.28±0.8	1.14±0.09	29.69± 0.19
D8	0.44±0.045	0.51±0.04	13.72±0.1	1.15±0.05	27.36±0.23
D9	0.45±0.04	0.52±0.1	13.46±0.8	1.15±0.09	29.32±0.16

Percentage Drug entrapment efficiency of Docetaxel ranged from 62.66 to 88.66% for microspheres containing albumin and chitosan. The drug entrapment efficiency of the prepared beads increased progressively with an increase in proportion of the respective polymers. Increase in the polymer concentration increases the viscosity of the dispersed phase. The particle size increases exponentially with viscosity. The higher viscosity of the polymer solution at the highest polymer concentration would be expected to decrease the diffusion of the drug into the external phase which would result in higher entrapment efficiency. The % drug entrapment efficiency of the prepared beads is displayed in Table-2 and fig-1.

Table-2 Percentage yield and percentage drug entrapment efficiency of the prepared Microspheres

S.No.	Formulation code	% yield	Drug Content (mg)	%Drug entrapment efficiency
1	**D1**	82.2	74.2	62.41
2	**D2**	82.41	78.68	65.16
3	**D3**	84.17	77.47	67.62
4	**D4**	84.62	79.2	70.18
5	**D5**	83.29	75.6	76.21
6	**D6**	84.61	77.4	78.17
7	**D7**	87.19	82.9	88.24
8	**D8**	86.42	80.7	86.19
9	**D9**	84.16	79.14	83.48

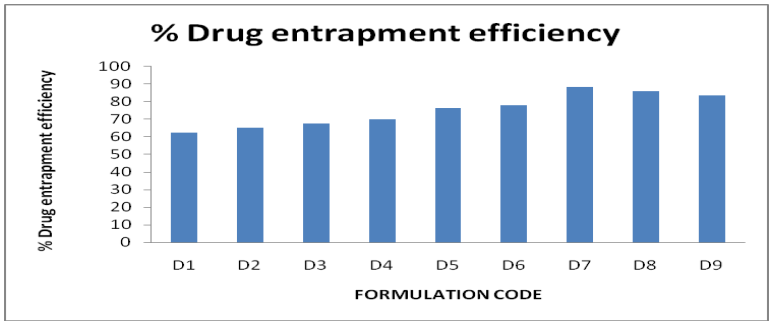

Fig-1 Drug entrapment efficiency graph for D1-D9 formulations

Among all the formulations D7 shows more sustained after 9 hourwhere as all other shows optimum sustainity like D7 but D7 shows highest drug release at 12Hr where as remaining all other shows less percent of drug release so D7 was optimized as best formulation (Fig-2, 3 and 4).

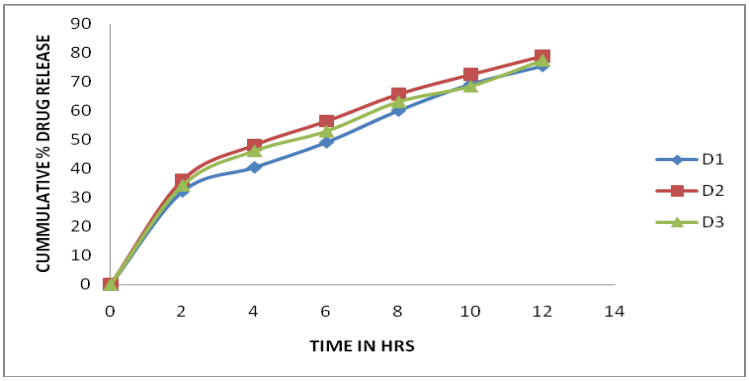

Fig-2 Dissolution profile of Docetaxel Microspheres (D1, D2, D3) formulations.

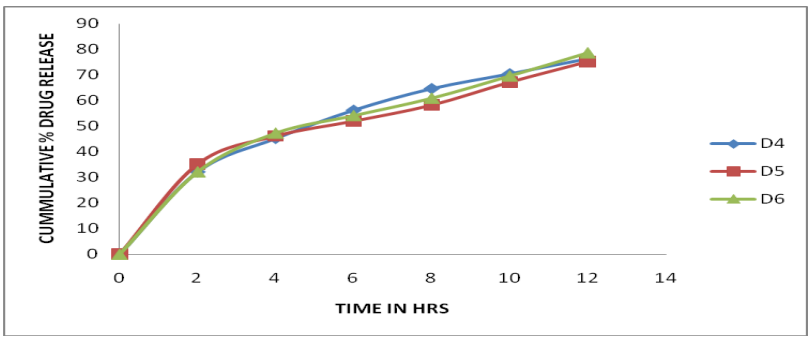

Fig-3 Dissolution profile of Docetaxel Microspheres (D4, D5, D6) formulations

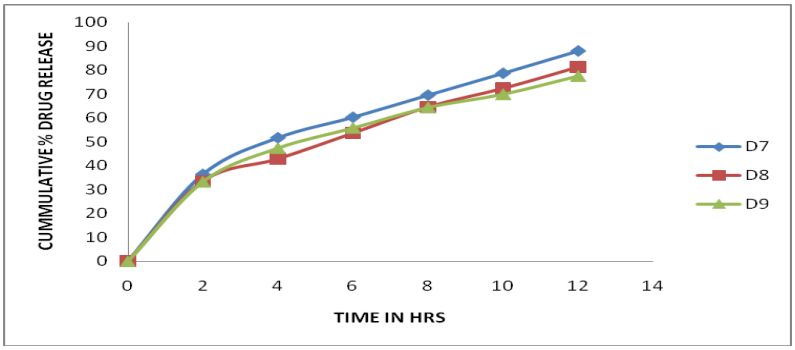

Fig-4 Dissolution profile of Docetaxel Microspheres (D7, D8, D9) formulations

The D7 formulation follows first order kinetics with R^2 value of 0.9766 and also follows Higuchi model with an R^2 value of 0.9985 and also follows non fickanian model of drug release.

CONCLUSION

The present study has been asatisfactory attempt to formulate floating microspheres of Docetaxel, a new anti-mitotic chemotherapy medication used mainly for the treatment of breast, ovarian, and non-small cell lung cancer. Drug giving a controlled release of the drug. From the experimental results it can be concluded that, FT-IR study shows no significant shifting of the peaks there for it confirms the short term stability of the drug in the beads. Biocompatible

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REFERENCES

1.Yie W. Chien, 'Rate-controlled Drug Delivery Systems'. *Ind. J. Pharm. Sci*., 1988; Mar-April: 63-65.

2.Thomas Wai-Yip Lee and Joseph R. Robinson, "*Controlled / Release Drug-Delivery Systems*", Chapter 47 in 'Remington's Pharmaceutical Sciences', 20th Edition, Mack Publishing Company, Volume-I, 2000; 903-929.

3.D. M. Brahmankar, Sunil B. Jaiswal., *Biopharmaceutics and Pharmacokinetics a Treatise*, First edition, Vallabh Prakashan Pitampura, Delhi-2001; 337-341.

4. Herbert A. Lieberman, Leon Lachman, and Joseph B. Schwartz *Pharmaceutical dosage forms* IInd Edition Volume-I, 7.

5.Arul B. and R. Kothai, "Formulation and evaluation of chitosan microspheres containing isoniazid", *Ind. J. Pharm. Sci*., 2003; 66 (5), 640.

6. Govindrajan G., and K. Muttusamy, "Formulation and evaluation of floating hollow microspheres of lansoprazole",*Ind. J. Pharm. Sci*., 2004; 66 (4), 486.

7.Rahul Nair, B.Haritha Reddy application of chitosan microspheres as drug carriers , *journal of pharmaceutical science and research* vol 1(2), 2009, 1-12.