International Journal of Advanced Research and Review

www.ijarr.in

FORMULATION AND EVALUATION OF MICROCAPSULES OF FURAZOLIDONE

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ABSTRACT

The objective of the present study was to develop Furazolidone prolonged release microcapsules by solvent evaporation method. This sustained release of microcapsules is additionally influenced by the formulation of latest biodegradable polymer HPMC and Ethyl cellulose, hence drug release pattern. The ready microcapsules were subjected to numerous pre and post formulation studies. Prepared microcapsules were evaluated for the particle size, percentage yield, entrapment efficiency, wall thickness, estimation of drug content and in vitro drug release studies. Results of the present study indicate that Furazolidone microcapsules can be successfully designed to develop sustained drug delivery, that reduces the dosing frequency and their by we can increase the patient compliance.

Keywords: Furazolidone, Ethyl Cellulose, HPMC, Microcapsules, Solvent evaporation.

INTRODUCTION

Microencapsulation is a useful method which, prolongs the duration of drug effect significantly and improves patient compliance. Eventually the total dose and few adverse reactions may be reduced since a steady plasma concentration is maintained.[1]

Furazolidone is used to treat bacterial and protozoal infections. It works by killing bacteria and protozoa (tiny, one-celled animals). Some protozoa are parasites that can cause many different kinds of infections in the body. Furazolidone is taken by mouth. It works inside the intestinal tract to treat cholera, colitis, and/or diarrhea caused by bacteria, and giardiasis. This medicine is sometimes given with other medicines for bacterial infections. Furazolidone may cause some serious side effects when taken with certain foods, beverages, or other medicines.[10]

Microencapsulation is defined as the application of a thin coating to individual core materials that have an arbitrary particle size range between 5 and 5000 um. Microencapsulation is widely used in the pharmaceutical and other sciences to mask tasted or odors, prolong release, impart stability to drug molecules, improve bioavailability, and as multi particulate dosage forms to produce controlled or targeted drug delivery. It is therefore, a rapidly expanding technology for achieving sustained-release dosage forms.[2]

The solvent evaporation method of microencapsulation involves the use of emulsification of a solution containing polymer and drug with an additional medium in which the drug and polymer

cannot dissolve. The technique is relatively simple and has been used to prepare microcapsules of a variety of compounds using several different polymeric materials.[3, 4]

Reason for the selection of furazolidone microcapsules are Extended duration of activity for short half life drugs, Decreased toxicity, and reduction of required dose, Optimized therapy and better patient compliance, Predictable and reproducible release rates, of maximizing the bioavailability of conventional drugs with minimum side effects.

The aim of this work was to develop microcapsules of Furazolidone by solvent evaporation technique. Due to prolonged release.

MATERIALS

Furazolidone was obtained as a gift sample from the Plethico Pharmaceutical Limited, India. Prolonged release polymer Ethyl cellulose, HPMC were supplied as gift sample by Central Drug House Ltd., Liquid paraffin, petroleum ether was obtained from Rankem Lab. Reagent, Span 80 were supplied from Loba Chemise Pvt. Ltd., Chloroform was supplied from Molychem. All other chemicals and reagent used in this study were of analytical grade.

Preformulation Study:

Methods:

Physical appearance: The supplied sample of Furazolidone was visualized.

Identification of drug:

- **Identification by UV spectrophotometer:** The identification of drug was done by UV spectrophotometer method. The 25 mg of drug was dissolved in 100 ml of distilled water and scanned in UV. The absorbance was taken at 367 nm. The highest peak of Furazolidone and spectra was recored.[11]

- **Melting point determination:** Melting point determination of furazolidone was done by using melting point apparatus. In this method the presealed capillary was filled by the small amount of drug. Then capillary and thermometer was placed in placed point apparatus. Then see capillary for melting the dug. The temperature were noted when the drug start to melt and the drug till complete melt.

- **Solubility determination:** The solubility determination of furazolidone was carried out in water, chloroform, liquid paraffin, petroleum ether, ethanol. The excess of drug was added gradually to 5 ml of each solvent contained in 10 ml of vials and vials were sealed with rubber closures and aluminum seals. The vials shaken for 12 hr and allowed to equilibrate for 24 hrs. undistributed. The solution containing excess of drug were centrifuged and filtered through whatmen grade filter papers. Aliquots of filtrate were suitably diluted and the dilutions were analyzed on UV- visible spectrophotometer.

- **Partition coefficient determination:** Accurately weighed 20 mg of drug was added into a mixture of 10 ml of water and 10 ml of n- octanol, placed in a separating funnel. It was shaken for 15 min. and allows standing 24 hrs. The phases was separated and filtered through whatman grade filter paper, and the amount of drug in phases was measured in UV- visible spectrophotometer. The partition coefficient were calculated as the ration of the concentration of drug in oil phase and water phase.[14,15]

- **Determination of λmax:** The stock solutions were suitably diluted with distilled water so as to contain 10 µg/ml of Furazolidone. The solution were scanned in the UV region between 200-400 nm and found that furazolidone exhibited λmax at 367 nm.[12]

- **Preparation of calibration curve:** The standard stock solution of Furazolidone was prepared by dissolving 25 mg of drug in 100 ml of distilled water to get a concentration of 250 µg/ml. From this stock solution 0.5, 1, 1.5, 2 2.5, 3, 3.5, 4, 4.5, 5 ml solution was taken and dilute up to 10 ml with distilled water to get the desired concentration range (5-50 µg/ml). The linearity was observed in the concentration range of 5 to 50 µg/ml for furazolidone. The absorbance were observed against distilled water as blank and the calibration carve was plotted between concentration (x-axis) and absorbance (y-axis).[13]

- **Drug excipient compatibility study:** A small amount of drug substance with excipient that is, physical mixture of the drug and excipients in ration (1:1) were prepared to have maximum in tractions between them was placed in vial and rubber stopper was placed on the sealed properly. A storage period of 2 weeks for 60^0c and the sample was retained for 2 months at 40^0c. After storage the sample were observed physically for liquification, cracking, odour, or gas forming, dis coloration.

- **Particle size analysis:** Determination of average particle size of the furazolidone was carried out by the optical microscopy method. A minute quantity of furazolidone were dispersed in liquid paraffin and then spread on clean glass slide and average sizes of furazolidone were determined.[14]

Formulation of Microcapsules

Microcapsules were prepared by solvent evaporation method. Various formulations of microcapsules were prepared using gradually increase ethyl cellulose, HPMC concentration. In this method the polymer is dissolved in a definite volume of internal phase (Chloroform, Ethanol) and then the drug is also dissolved in the polymer solution. This drug polymer solution is then dispersed in an external medium (Liquid paraffin) consisting 1% span 80 in a 500 ml of beaker. The whole system was stirred at a 800-1000 rpm using mechanical stirrer equipment with three propellers for 3-4 hrs at 25-40^0C to ensure the evaporation of the solvent. The smooth-walled, rigid and discrete microcapsules were formed. The microcapsules were collected by decantation and the product was washed with petroleum ether (40-60^0C), four times and dried at room temperature for 3 hrs.[5,6,7]

Composition of Microcapsules

Table 1. Composition of Microcapsules of Furazolidone

Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)
Furazolidone	**100**	**100**	**100**	**100**	**100**	**100**
Ethyl cellulose	**100**	**-**	**200**	**-**	**300**	**-**
HPMC	**-**	**100**	**-**	**200**	**-**	**300**

Evaluation of Furazolidone Microcapsules

- **Particle size analysis:** Determination of average particle size of the furazolidone microcapsules was carried out by the optical microscopy method. A minute quantity of microcapsules were dispersed in liquid paraffin and then spread on clean glass slide and average sizes of microcapsules were determined in each batch.[14]

- **Percentage yield:** The total amount of microcapsules obtained was weighed and the percentage yield calculated taking into consideration the weight of the drug and polymer.
  % Yield = (Practical yield / Theoretical yield) x 100

- **Estimation of drug content:** Furazolidone drug content in the microcapsules was calculated by UV spectrophotometric (Shimadzu 1700) method. A sample of microcapsules equivalent to 100 mg was dissolved in 25 ml ethanol and the volume was adjusted up to 100 ml using phosphate buffer of pH 6.8. The solution was filtered through Whatman No. 1 filter paper. Then the filtrate was assayed for drug content by measuring the absorbance at 365 nm after suitable dilution.

- **Entraptment efficiency:** Entrapment efficiency was calculated using the formula:
  % Entrapment efficiency = (Estimated % drug content in microcapsules / Theoretical % drug content in microcapsules) x 100

- **Wall thickness:** Wall thickness of furazolidone microcapsules was determined by -
  Wall thickness = Particle size of Drug – Particle size of Microcapsule

- **In vitro drug release:** Drug release was studied by using USP type II dissolution test apparatus in phosphate buffer of pH 6 (900ml). The paddle speed at 100 rpm and bath temperature at 37 ± 0.5^0c were maintained throughout the experiment. A sample of microcapsules equivalent to 100 mg of furazolidone was used in each test. Aliquot equal to 5 ml of dissolution medium was withdrawn at specific time interval and replaced with

fresh medium to maintain sink condition. Sample was filtered through Whatman No. 1 filter paper and after suitable dilution with medium, the absorbance was determined by UV spectrophotometer (Shimadzu 1700) at 365 nm. [16,18,19]

RESULT AND DISCUSSION

- **Organoleptic properties:**
  Colour **:** Pale Yellow
  Crystalinity **:** Crystaline
  Taste **:** Metallic
  Odour **:** Odourless

- **pH determination:** The pH value of furazolidone was found to be 6.0 which is nearly to standard. So it shows that the drug is acidic.

- **Melting Point:** The melting point of was 251^0-256^0C which is nearly to standard of Furazolidone. So it shows that the drug is pure.

- **Solubility properties:**

Table 2. Solubility properties of Furazolidone

Solvents (10ml)	Solubility properties of the drug (10mg)
Water	++++
Chloroform	+++
Liquid Paraffin	++++
Petroleum Ether	+
Ethanol	+++

\+ Insoluble
++ Poorly soluble
+++ Slightly soluble
++++ Freely soluble

Its shows the Furazolidone is excellent soluble in aqueous organic solvent.

- **Partition coefficient:** The partition coefficient of Furazolidone was found to be 0.99. The result has been shown that the drug is hydrophilic.

- **Particle size determination:**
  The result of the microscopic evaluation of particle size of the furazolidone particles are given below in table-

Table 3. Particle size determination of Furazolidone

S.No	Size Range	Mid point (M.P)	No. of particle (N)	M.P × N	M.P×N×L.C
1	0-1	0.5	04	2	2.6
2	1-2	1.5	09	13.5	17.55
3	2-3	2.5	18	45	58.5
4	2-4	3.5	22	77	100.01
5	4-5	4.5	25	112.5	135
6	5-6	5.5	22	121	157.3
			∑n= 100		∑d=470.96

Least count (L.C) = 1.3

Particle size of Furazolidone = ∑d \ ∑n

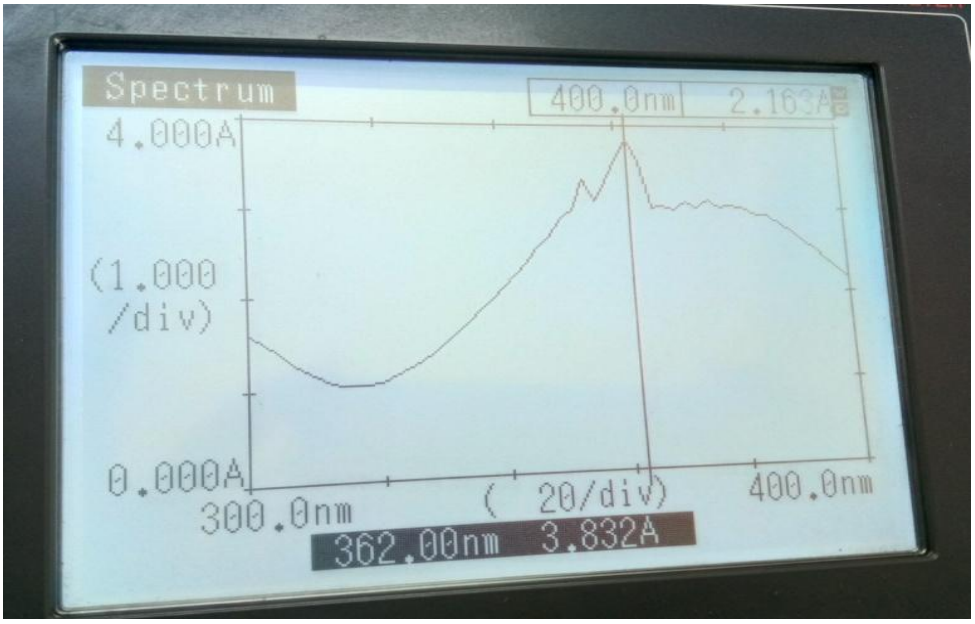
= 470.96\ 100

= 4.70

Particle size was found to be 4.70 µm show that drug particle are distributed in range of 1-6 µm and maximum number of particle are present in size range of 4-6µm. This distribution pattern also indicates that the drug is amorphous in nature.

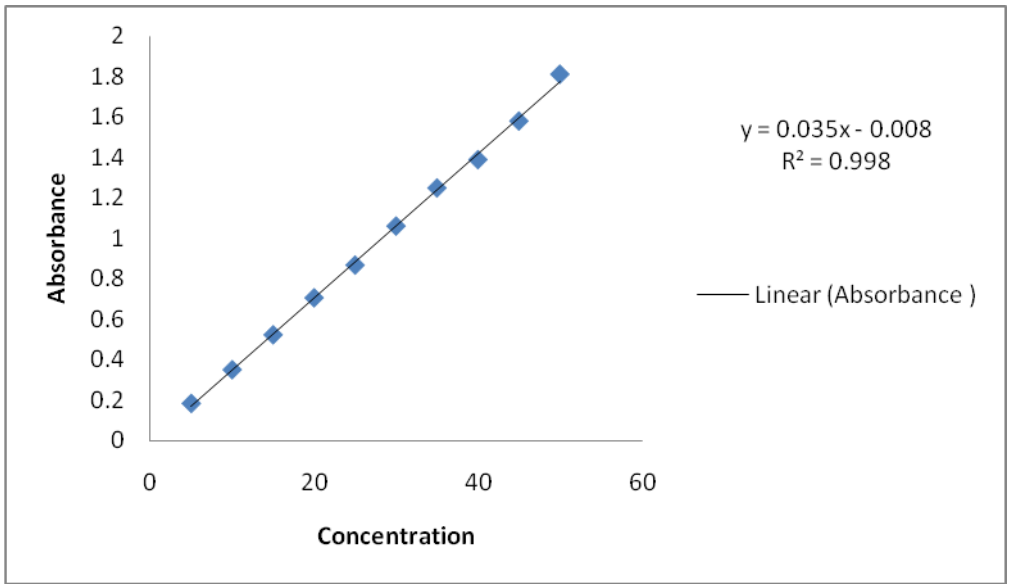
- **Absorption maximum (λmax):** The solution were scanned in the UV region between 200-400 nm and found that furazolidone exhibited λmax at 362 nm which is nearby to the standard value of furazolidone. This so the drug is pure.

- **Identification of drug:** The identification of drug was done by UV spectrophotometer method. The highest peak showed at 362 nm which is nearby to the standard value of furazolidone. This so the drug is pure.



(Fig. 1. Identification Curve of Furazolidone)

Calibration curve:



(Fig. 2. Calibration Curve of Furazolidone)

Equation:-

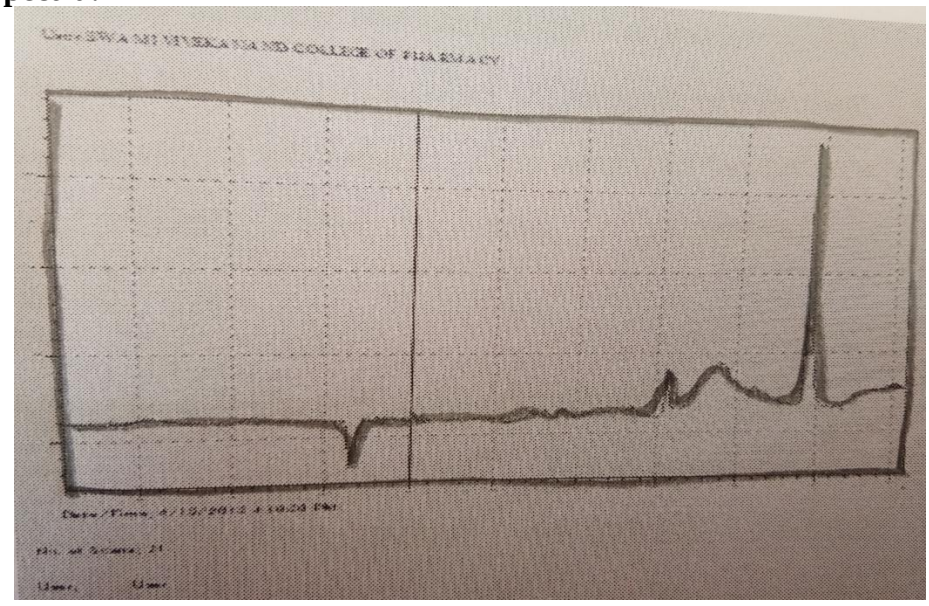
Y = 0.035x+0.008

R^2= 0.998

X= Concentration in micro gram

For preparation of standard curve, solution of the drug sample were prepared in distilled water and there absorbance were measured at 362 nm the linearity range were found to be 5-50 µg/ml. The furazolidone obey Beer's law in the range 5-50 µg/ml.

- **IR Spectra:**



(Fig. 3. IR Spectra of Furazolidone)

IR Spectrum of drug sample has been interpreted and correlate with standard IR spectrum of furazolidone. There is no change in functional group of drug sample or same with standard shown in figure. It show that the drug sample is furazolidone.

- **Drug excipients compatibility study:**

Table 4. Furazolidone with Polymer Compatibility

Additives (100 mg each with drug)	**Observation at 60^0c for 2 week**	**Remarks**
Furazolidone	No change	Accepted
Drug + Ethyl cellulose	No change	Accepted
Drug + HPMC	No change	Accepted

- **Particle size:** The particle size of microcapsules varied somewhat among the formulation variation in the method of preparation of various formulations. Particle size was found to be satisfied when prepared by solvent evaporation method. Microcapsules prepared by solvent evaporation method showing lesser size than other methods. The mean particle size of the microcapsules significantly increases with increasing polymer concentration. It was observed that, on increasing the polymer amount the average particle size increased. The particle size of formulations in the range between 4.32 µm to 6.90 µm.

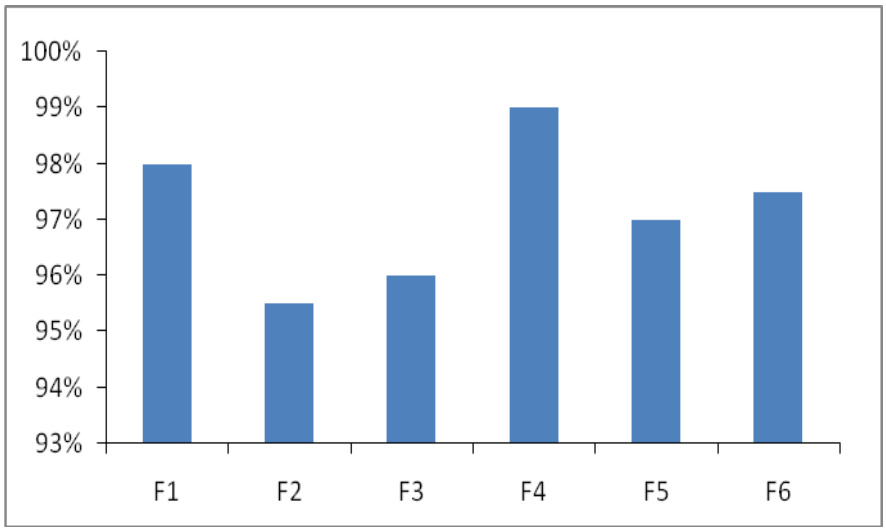
Table 5. Particle Size of Microcapsules of Furazolidone

Formulations	F1	F2	F3	F4	F5	F6
Particle size (µm)	4.32	5.61	5.95	6.21	6.58	6.90

- **Percentage yield:** The maximum percentage yield was found to be range between 95.5 to 99%. Formulation F4 is better than the other formulations because its percentage yield 99%.

Table 6. Percentage yield of Microcapsules of Furazolidone

Formulations	F1	F2	F3	F4	F5	F6
Percentage yield	98 %	95.5 %	96 %	99 %	97 %	97.5 %



(Fig. 4. Percentage Yield of Formulations)

- **Estimation of Drug Content :** The amount of Furazolidone estimated from drug content microcapsules different formulations was found to be range of 72 % to 93 %. The F5 and F6 formulations are better than other formulations because in this formulations increasing the polymer concentration.

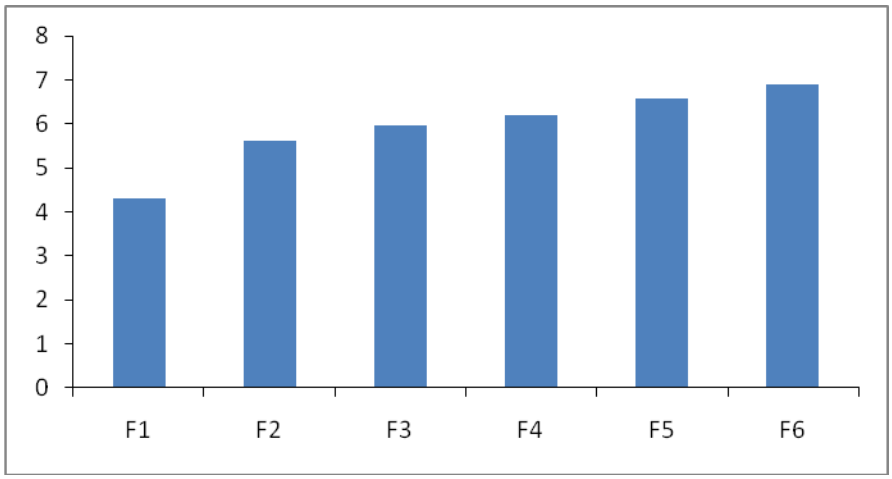
Table 7. Drug Content of Microcapsules of Furazolidone

Formulations	F1	F2	F3	F4	F5	F6
% Drug content	93 %	87 %	84 %	79 %	76 %	72 %

- **Drug entrapment efficiency:** The drug entrapment efficiency was found in the range between 63.79 – 93.66 %. The F1 and F2 formulations is better than other formulation because in this formulations are similar the drug and polymer ratio.

Table 8. Drug entrapment efficiency of Microcapsules of Furazolidone

Formulations	F1	F2	F3	F4	F5	F6
% Entrapment efficiency	93.66 %	86.78 %	78.73 %	75.28 %	67.24 %	63.79 %

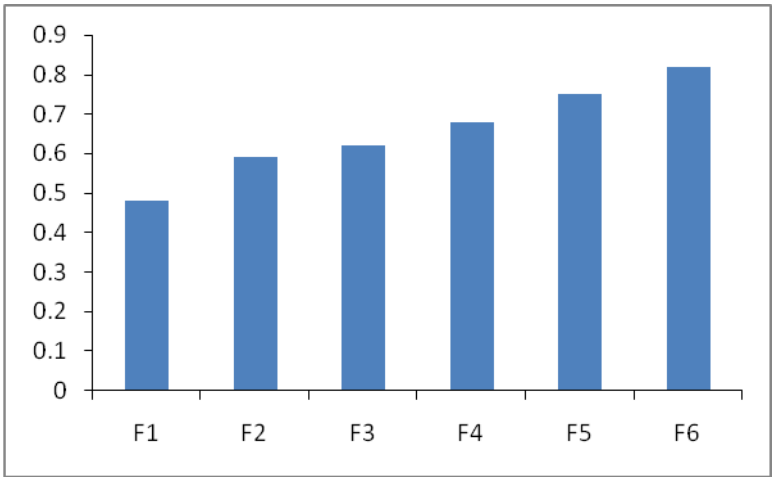


(Fig. 5. Drug Entrapment Efficiency of Formulatios)

- **Wall thickness:** The wall thickness of furazolidone microcapsules formulations was found to be in the range between 0.48 to 0.82 µm. The concentrations of polymer are increasing in formulations than the wall thickness is also increases.

Table 9. Wall thickness of Microcapsules of Furazolidone

Formulations	F1	F2	F3	F4	F5	F6
Wall thickness (µm)	0.48	0.59	0.62	0.68	0.75	0.82



(Fig. 6. Wall Thickness of Formulatios)

- **In vitro Drug release studies:** All the six formulation of prepared microcapsules of Furazolidone were subjected to in vitro release studies these are carried out in dissolution medium (PBS pH 6).

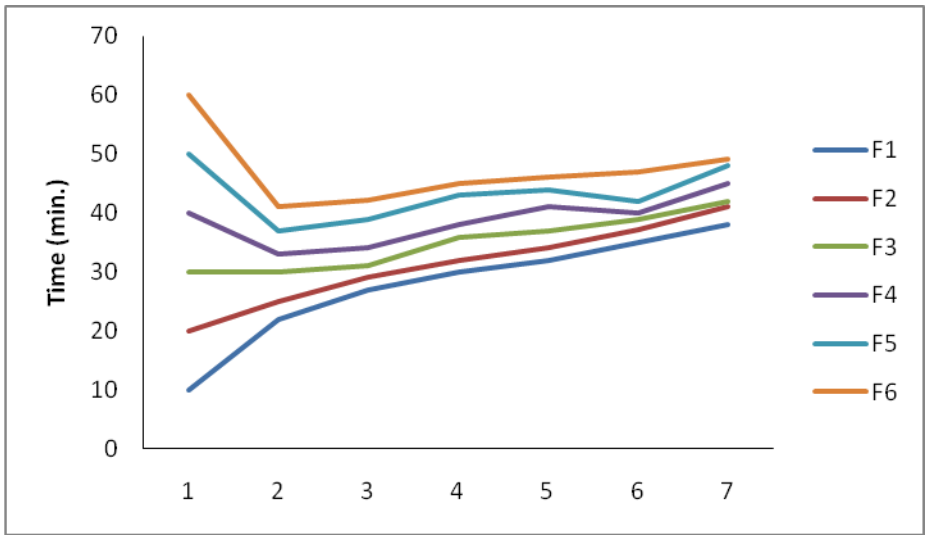
Cumulative % drug released of microcapsules formulations F1 – F6.

Table 10. Drug Release of Microcapsules of Furazolidone

Time Interval (min.)	F1	F2	F3	F4	F5	F6
10	22	27	30	32	35	38
20	25	29	32	34	37	41
30	30	31	36	37	39	42
40	33	34	38	41	40	45
50	37	39	43	44	42	48
60	41	42	45	46	47	49

Result shows that formulation F5 having quick release in 12.5±0.69 second.
It indicates that amongst the prolonged release polymer ethyl cellulose and HPMC show better released profile microcapsules.

In vitro drug release was found between 86 – 98 % within 30 min of the study. The formulation F5 and F6 containing ethyl cellulose and HPMC in equal proportion have shown highest drug release (98±0.88) within 30 min compared to other formulations.



(Fig. 7. In Vitro Drug Release of Formulations)

The microcapsules are packed in suitable packaging and stored under the following condition for a period as prescribed by ICH guidelines for accelerated studies. In order to determine the change in particle size, percentage yield, wall thickness, entrapment efficiency, in vitro drug release studies, estimation of drug content study of different formulation.

CONCLUSION

- Formulation of microcapsules of Furazolidone for the prolonged release of drug.
- Formulations F4 and F5 were found to be best among all other formulation.
- Biodegradable hydrophilic polymer Ethyl cellulose and HPMC is suitable for the preparation of microcapsules for the sustained release.
- Viscosity of polymer plays the major role in formulation of microcapsules of furazolidone.
- There is no interaction between the polymer and drug of microcapsules of furazolidone.
- Microcapsules of Furazolidone can be used as anti bacterial agents.
- Improved the patient compliance.

ACKNOWLEDGEMENTS

Author's are thankful to Swami Vivekanand College of Pharmacy, Indore (India) authority for providing suitable research laboratory to carry out this project work and it also thanks to the Plethico Pharmaceutical Limited, India, for providing gift sample of Furazolidone and thanks to B. M. College of Pharmaceutical Research and Education.

REFERENCES

1. Venkatesan P. and Manavalan R., "Microencapsulation: A Vital Technique In Novel Drug Delivey System", Journal of Pharmaceutical Sciences and Research, Vol. 1, Issue 4, 2009, 26-35.
2. Bansode S. S., Banarjee S. K., Gaikwad D. D. and Jadhav S. L.,"Microencapsulation", International Journal of Pharmaceutical Sciences Review and Research, Vol. 1, Issue 2, Mar-Apr. 2010, 38-43.
3. Hamid M., Qazi H. J., Waseen S. and Zhong F., "Microencapsulation Can Be a Novel Tool in Wheat Flour with Micronutrients Fortification: Current Trends and Future Application", Czech Journal Food Sciences, Vol. 31, 2013, 527-540.
4. Mishra D. K., Jain A. K. and Jain P. K., "Various Techniques of Microencapsulation", International Journal of Pharmaceutical and Chemical Sciences, Vol. 2, Issue 2, Apr-Jun 2013, 962-977.
5. Tiwari S., Goel A., Jha K. K. and Sharma A., "Microencapsulation Techniques and Its Application", The Pharma Research, A Journal, Vol. 3, 2010, 112-116.
6. Dubey R. and Rao K. U. Bhasker, "Microencapsulation Technology and Applications", Defense Science Journal, Vol. 59, Issue 1, Jan. 2009, 82-95.
7. Muthuprasanna P., "Microencapsulation", International Journal of Pharma and Bio Sciences, Vol. 3, Issue 2, Jan.-Mar. 2012, 509-531.
8. Umer H. and Nigam H., "Microencapsulation: Process, Techniques and Applications", International Journal of Research in Pharmaceutical and Biomedical Sciences, Vol. 2, Issue 2, Apr.-Jun. 2011, 474-481.
9. Naga M. and Banji D., "Microencapsulation", International Journal of Pharmaceutical Sciences Review and Research, Volume 5, Issue 2, Nov.-Dec.2010, 58-62.

10. Venkateswaramurthy N. and Sambathkumar R., "Formulation and in vitro evaluation of furazolidone mucoadhesive microspheres", International Journal of Pharmacy and Pharmaceutical Sciences, Vol 2, Issue 3, 2010, 104-106.
11. Chemate S. Z., Dongare U. S., Jadhav S. A. and Jadhav M. B., "Validated spectrophotometric methods for simultaneous estimation of Metronidazole and Furazolidone in pure and in tablet dosage form", International research journal of Pharmacy, 2012, 461-464.
12. Naidu N. V., "Spectrophotometric Method for the Determination of Furazolidone in Pharmaceutical Formulations and Human Blood Samples with MBTH", International Journal of Science and Research, Volume 4 Issue 5, May 2015, 1026- 1031.
13. Mittan D. S., "Development and validation of new colorimetric method for the estimation of furazolidone in bulk and solid dosage form ", Analytical chemistry An Indian Journal, Volume 7, Issue 8, August 2008, 609-611.
14. Lachman L. "The Theory Practice of Industrial Pharmacy" 2nd Edition, Varghee publishing House Bombay ,412-429.
15. Jain N. K., "Pharmaceutical product development", 2006, First edition, Published by Satish kumar jain and produced by V.K. jain for CBS publisher and distributers Pvt. Ltd New Delhi, 61-111.
16. Yadav A. V, Shete A. S, Dabke A. P. and Shinde V. R., "Formulation and In-vitro Evaluation of Aceclofenac Microencapsules" International Journal of PharmTech Research, Vol.1, Issue 2, Apr.-June 2009, 135-138.
17. Gustafson J. H., Weissman L. and Weinfeld R. T., "Clinical bioavailability evaluation of a controlled release formulation of diazepam", J. Pharmacokinet Biopharm, Volume 9, 1981, 679-691.
18. Emami J. and Varshosaz J., "Preparation and evaluation of a sustained-release suspension containing theophylline microcapsules" African Journal of Pharmacy and Pharmacology, Vol. 6, Issue 28, 29 July, 2012, 2091-2099.
19. Chowdary K. P. R. and Dana S. B., "Preparation and evaluation of ethylcellulose coated microcapsules for controlled release of Diclofenac" Research Journal of Pharmaceutical Biological and Chemical Sciences, Volume 2, Issue 1, January – March 2011, 608-615.
20. Bolourtchian N., Karimi M. and Aboofazeli R., "Preparation and characterization of Ibuprofen microspheres", J. Microencap., 2005, Volume 22, Issue 5, 529-538.
21. Yamuda T. and Machida Y., "Sustained release ketoprofen microparticles with ethyl cellulose and carboxymethylethyl cellulose", J. Controlled Release, 2001, Volume 75, Issue 3, 271-282.
22. Rasal A., Mahajan H. S., Shaikh H. T. and Surana S. J., "Development and Characterization of Nasal Mucoadhesive Microemulsion of Sumatriptan Succinate", Indian Journal of Novel Drug Delivery, Vol. 2, Issue 3, Jul-Sep. 2010, 103-108.
23. Pandya H. V., "Formulation and Evaluation of microcapsules of triexyphenidyle hydrochloride by solvent evaporation method", International Journal of Pharmaceutical Sciences and Research, 2012, Volume 3, Issue 2, 539-544.