



Formulation and Evaluation of extended release Multiparticulate drug Delivery System

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Abstract: The aim was Formulation and Evaluation of extended release Multiparticulate drug Delivery System Extended-release drug delivery system is designed to achieve a prolonged therapeutic effect by continuously releasing the medicament over an extended period of time. Such system extends the duration time over a therapy, reduce side effects and increase the safety and patient compliance by reducing frequency of dosing. In present study an attempt has made to prepare extended-release matrix pellets by extrusion – spherization method

Keywords: Multiparticulate drug Delivery System, rifampicin, HPMC, MCC

Introduction:-

The oral route is the most popular route used for administration of drugs, which is due in part to the ease of administration and to the fact that gastrointestinal physiology offers more flexibility in dosage form design than most other routes. The term sustained release, prolonged release, modified release, extended release or depot formulation are used to identify drug delivery system that are designed to achieve or extend therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.⁽¹⁾ The advantages of administering a single dose of a drug that is released over an extended period of time, instead of drug numerous doses, have been obvious to the pharmaceutical industry for some time. The desire to maintain a near constant or uniform blood level of drug often translates into better patient compliance as well as enhanced clinical efficacy of drug for its intended use. Because of increased complication and expense involved in marketing of new drug entities, has focused greater attention on development of sustained or controlled release drug delivery systems.⁽²⁾ The multi-particulate drug delivery systems are suitable for oral formulation to achieve controlled or delayed release. It has advantages like low dose dumping, flexibility of blending to attain different release pattern and for short gastric residence time. Therefore, Multi-particulate drug delivery system (MPDDS) provides opportunities in designing controlled and delayed release oral formulation. Multiparticulate drug delivery systems are oral dosage forms consisting of multiplicity of small discrete units, in which active substance is present as a number of independent It is based on subunits such as granules, beads, microspheres, pellets, spheroids and mini-tab. Pellets are defined as spherical/ semi-spherical, free flowing solid units with a narrow size distribution, typically in diameter between 0.5-2.0 mm. Palletization technique is used to produce pellets. Sustained release systems include any drug delivery system that achieves slow release of drug over an extended period of time. If the system is successful in maintaining constant drug levels in the blood or target tissue, it is considered as a controlled-release system.⁽³⁾ There is certain consideration for the preparation of extended-release formulation: If the active compound has a long half-life, it is sustained on its own, If the pharmacological activity of the active is not directly related to its blood levels, If the absorption of the drug involves an active transport and if the active compound has very short half-life, then it would require a large amount of drug to maintain a prolonged effective dose.^(4,5)

Method of preparation of pellets

- Extrusion-spherization.
- Drug layering.
- Globulation or droplet.
- Spray congealing.

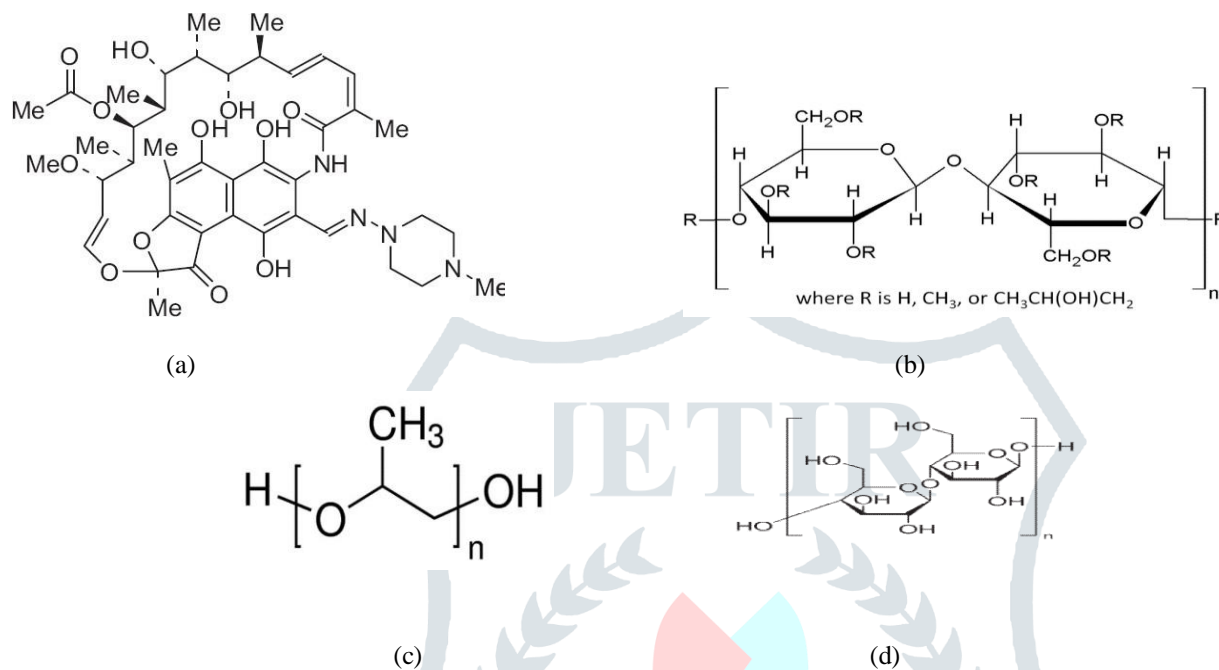


Figure 1 : Structure of (a) rifampicin (b) HPMC and (c) Polyethylene glycol (d) MCC

2. PREPARATION OF extended-release matrix- pellets by extrusion spherization :

Four formulations of matrix pellets contain rifampicin, HPMC, PEG4000, MCC pH102, PVP and lactose were prepared by extrusion-spherization process. The drug, sustained release polymer i.e. HPMC, PEG-4000 and palletization aid mcc, lactose were mixed in mortar and triturate for 5 min then the pvp and water as binder solution was added to achieve a consistency of damp mass. The prepared damp mass was passed through extrudate. The extrudate were then sponerized in a sponerized with rotation plate for 15 min. The resultant matrix pellets were dried at room temperature.

Ingredients (mg)	F1	F2	F3	F4
Rifampicin	300	300	300	300
HPMC	50	50	75	75
PEG-4000	50	75	50	75
MCC ph 102	85	85	85	85
PVP	15	15	15	15
Lactose	21	21	21	21
Water	q.s	q.s	q.s	q.s

Table 1 : preparation of pellets

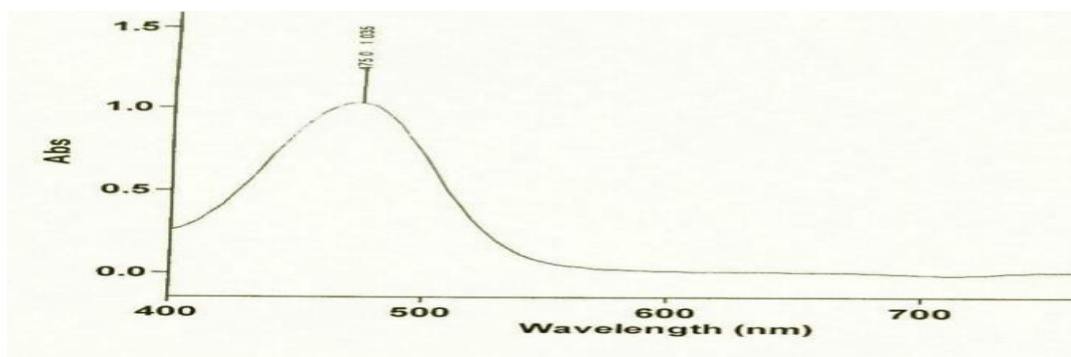
3. Results and discussion

Preformulation test :

Physical Charateres:-

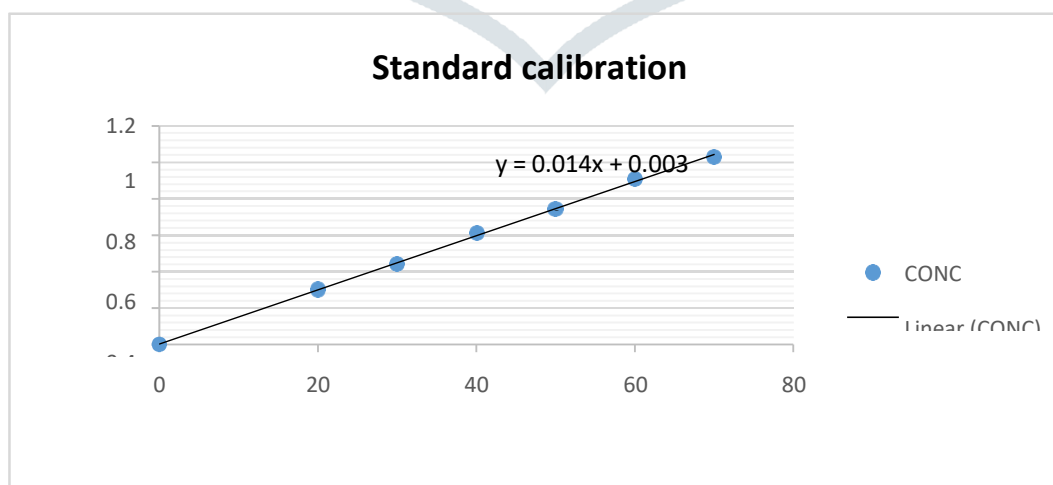
Taste	Observation
Colour	Reddish brown
Odour	Odorless
Melting point	180-183°C

Determination of λ max of Rifampicin :-



Standard calibration

Conc.(μ /ml)	Absorbance at 475
0	0
20	0.3037
30	0.4409
40	0.6109
50	0.7435
60	0.9085
70	1.0309



Evaluation of prepared matrix pellets

Batches	Angle of Repose(ϕ) \pm S.D	Bulk density	Tapped density	Car's index(%)	Hausner's ratio	Friability (%)
F1	27.68 \pm 0.4 8	0.32 \pm 0.01	0.35 \pm 0.01	11.65 \pm 2.4 6	1.22 \pm 0 .04	0.50 \pm 0.1 0
F2	21.10 \pm 2.8 4	0.25 \pm 0.01	0.28 \pm 0.01	10.58 \pm 2.4 6	1.11 \pm 0 .01	0.82 \pm 0.0 6
F3	18.36 \pm 0.9 6	0.28 \pm 0.01	0.31 \pm 0.01	8.49 \pm 1.18	1.08 \pm 0 .04	0.63 \pm 0.0 9
F4	17.15 \pm 0.3 3	0.30 \pm 0.01	0.32 \pm 0.02	7.10 \pm 1.72	1.07 \pm 0 .02	0.74 \pm 0.1 1

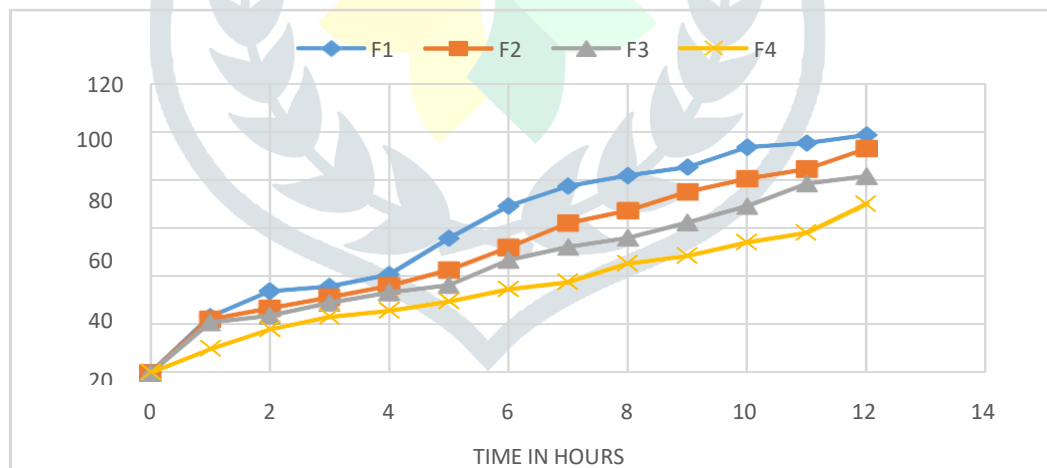
Percent Drug content:

Batches	Particle size(mm)	% drug content
F1	0.87 \pm 0.24	90.28 \pm 0.54
F2	0.94 \pm 0.19	98.23 \pm 0.86
F3	0.91 \pm 0.15	95.23 \pm 0.64
F4	0.86 \pm 0.21	92.16 \pm 0.62

In-vitro dissolution

% Drug release				
Time(hr)	F1	F2	F3	F4
0	0	0	0	0

1	23.35	22.3	20.91	9.88
2	33.93	29.76	23.75	18.02
3	35.87	35.33	29.06	23.25
4	40.79	36.15	33.36	25.69
5	55.86	49.73	36.44	29.59
6	69.21	59.06	46.74	34.62
7	77.49	66.22	52.24	37.68
8	81.82	71.38	56.04	45.39
9	85.40	75.12	62.47	48.53
10	93.58	80.61	69.21	54.15
11	95.38	84.62	78.48	58.16
12	98.69	93.17	81.61	68.28



Kinetics release

Mathematical Model					
Optimized Batch(F2)	Zero order	First order	Hixson Crowell	Korsmeyer Peppas model	Higuchi model
R²	0.9844	0.7407	0.8938	0.1714	0.9855
Slope	7.0403	0.0996	0.5965	0.6048	0.0356
Intercept	11.8904	0.9980	3.3416	-1.1853	0.3192

4. Conclusion

It was concluded that the polymer plays a major role in the formulation of extended release matrix pellets of Rifampicin. Finally, the study revealed that the release of drug was low when the matrix pellets contained higher concentration of polymers.

5. References :-

- 1) Gupta PK and Robinson JR. "Oral controlled release delivery". Treatise on controlled drug delivery. 1992; 93(2): pp 545-555.
- 2) Jantzen GM and Robinson JR. "Sustained and Controlled-Release Drug Delivery systems". Modern Pharmaceutics, 1995; 121(4): pp 501-502.
- 3) Jeevana J.B., Jyosna D, "Multi-particulate drug delivery systems using natural polymers as release retardant materials", International Journal of Pharmacy and Pharmaceutical Sciences, 2010; 6 (10): 61-65.
- 4) Wani MS. "Controlled Release System A Review"; Pharmaceutical Review. 2008; 6(1): pp 41-46.
- 5) Sahil husen IJ, Mukesh RP. "Pharmaceutical Controlled Release Drug Delivery Systems": A Patent Overview. Aperiito J Drug Designing & Pharmacology 2014; 1(2): pp 1-22.
- 6) Sampath Kumar KP, Debjit B, Shweta S, Shravan P, Dutta AS. "Sustained release drug delivery system potential". The Pharma Innovation 2012; 1(2): pp46-56
- 7) Sahil husen IJ, Mukesh RP, Alpesh DP. "Sustained Release Drug Delivery Systems": A Patent Overview. Aperiito J Drug Designing and Pharmacology 2014; 1(1): pp1-14.
- 8) Shalin AM, Gaikwad PD, Bankar VH, Pawar SP. "Sustained release drug delivery systems: a review". Int J Phama Res Dev 2011; 2(12):147-60.
- 9) Hayashi T. Formulation, study and drug release mechanism of a new Theophylline sustained release preparation, Int. J Pharm., 2005; 304: pp91-101.
- 10) Robinson M. Sustained Action Dosage Forms the Theory and Practice of Industrial Pharmacy 2nd edition, Philadelphia, Lea and Febiger, 1970
- 11) Jantzen GM., Robinson JR, "Sustained and controlled-release drug delivery system"s, in Banker GS, Rhodes CT (Eds.) Modern Pharmaceutics, Third Edition, Revised and Expanded, Drugs and the Pharmaceutical Sciences, Marcel Dekker, Inc., New York., 1995; 72: pp575-609.

- 12) Venkatraman S, Davar N and Chester A. "An overview of controlled release systems": Edited by Donald L Wise, New York, Marcel Dekker Inc. Handbook of Pharmaceutical controlled release Technology, 2000; pp 431-465.
- 13) Chien-Chi L., Metters A T. "Hydrogels for controlled release formulation- Network design and mathematical modeling". Advanced drug delivery reviews; 2006; 58: pp1379-1408.
- 14) Cox PJ, Khan KA., Munday DL, "Development and evaluation of a multipleunit oral sustained release dosage form for ibuprofen: preparation and release kinetics". Int. J. Pharm.; 1999; 193: pp 73 -84.
- 15) Kincl M., Meleh M., Veers M., Vrecer F. "Study of physiochemical parameters affecting the release of diclofenac sodium from lipophilic matrix tablets", Acta Chim Slov; 2004; 51: pp 409-425.

