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FORMULATION DEVELOPMENT AND EVALUATION OF CARBIDOPA CONTROL RELEASE MATRIX TABLETS

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ABSTRACT

Formulations that are able to control the release of drug have become an integral part of the pharmaceutical industry. In particular oral drug delivery has been the focus of pharmaceutical research for many years. This type of drug delivery has been at the centre of research due to its many benefits over conventional dosage. The focus of this review is on matrix tablets due to their widely use and simplicity of the formulation. This includes the discussion of of matrix tablets and factors affecting the drug release from these formulations. The mechanism of drug release from HPMC matrices is also discussed. The work describes studies carried out on preparation and evaluation of sustained release matrix tablets of carbidopa by using HPMC and GUAR GUM. Sustained drug delivery is a topic of current interest in pharmaceutical research and industry. There are a large no of polymers for use in sustained drug delivery. The two important polymers used for the present study are HPMC and GUARGUM. The specific objectives of the investigation are as follows.To prepare carbidopa matrix tablets by using different ratios of HPMC and guargum by using two factorial design.To prepare and evaluate the tablets for different parameters like hardness, weight variation, thickness, friability, in vitro dissolution. FTIR studies explains about the interaction between the drug and excipients.

Key words: *Sustained Release, Matrix Tablet, Diffusion, Carbidopa, Evalution studies*.

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INTRODUCTION

The major challenge in the development of new controlled release devices is to achieve optimal drug concentration at the site of action. To achieve optimal drug concentration at the site of action, liberation of the drug from the device must be controlled as accurately as possible.Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulation. Classification: Modified release dosage forms, Extended release e.g. controlled release, sustained

release and prolonged release and Delayed release e.g. enteric-coated tablets.[1-4]

Advantages of Controlled Release Drug Delivery Systems:

Therapeutic advantage: Reduction in drug plasma level fluctuation; maintenance of a steady plasma level of the drug over a prolonged time period, ideally simulating an intravenous infusion of a drug. [5]

Reduction in adverse side effects and improvement in tolerability: Drug plasma levels are maintained within a narrow window with no sharp peaks and with AUC of plasma concentration versus time curve comparable with total AUC from multiple dosing with immediate release dosage forms. [6]

Patient comfort and compliance: Oral drug delivery is the most common and convenient for patients, and a reduction in
dosing frequency enhances compliance.

Reduction in healthcare cost: The total cost of therapy of the controlled release product could be comparable or lower than the immediate release product. With reduction in side effects, the overall expense in Disease management also would be reduced. This greatly reduces the possibility of side effects, as the scale of side effects increase as we approach the maximum safe concentration. [7]

Avoid night time dosing: It is also good for patients to avoid the dosing at night time.

Matrix Tablets

Matrix technologies have often proven popular among the oral controlled drug delivery technologies because of their simplicity, ease in manufacturing, high level of reproducibility, stability of raw materials and dosage form, and ease of scale –up and process validation. Technological advancement in the area of matrix formulation have made controlled release product development much easier than before, and improved upon the feasibility of delivering a wide variety of drugs with different physicochemical and biopharmaceutical properties. [8-15]

Advantages of Matrix Tablets : Easy to manufacture, Versatile, effective and low cost, Can be made to release high molecular weight compounds

Disadvantages of the matrix systems: The remaining matrix must be removed after the drug has been released, The drug release rates vary with the square root of time. Release rate continuously diminishes due to an increase in diffusion resistance and/or a decrease in effective area at the diffusion front. However, a substantial sustained effect can be produced through the use of very slow release rates, which in many applications are indistinguishable from zero-order. [11-10]

Objectives of the study:

- The main objective of controlled release drug delivery systems was to ensure safety and to improve efficacy of drugs as well as patient compliance.
- So, they are designed to provide a therapeutic amount of drug on the specific-site of absorption, and then to maintain the desired drug concentration.
- This idealized objective constitutes the most important aspect of drug delivery, namely, *spatial placement and temporal delivery* of a drug.
- In recent years, numerous controlled release systems using alternative routes have been designed. However, the oral route still remains as the most desirable one.
- So, the bulk of research is directed to oral dosage forms: it allows complying with the temporal aspect of drug delivery. On the other hand, modeling of controlled release of a water-soluble drug from matrix systems has been widely investigated.
- The use of drug delivery formulations based on porous or 'channeled' polymeric materials has led to re-evaluation of the existing models.
- The work describes studies carried out on preparation and evaluation of sustained

release matrix tablets of carbidopa by using HPMC and GUAR GUM.

- Sustained drug delivery is a topic of current interest in pharmaceutical research and industry. There are a large no of polymers for use in sustained drug delivery. The two important polymers used for the present study are HPMC and GUARGUM. The specific objectives of the investigation are as follows.
- To prepare carbidopa matrix tablets by using different ratios of HPMC and guargum by using two factorial design.
- To prepare and evaluate the tablets for different parameters like hardness, weight variation, thickness, friability, *in vitro* dissolution.

Pre and Post Formulation Studies:

Angle of repose, carrs index, hausners ratio, bulk and tapped density, hardness, thickness, weight variation, friability and invitro dissolution. [25-40]

MATERIALS AND METHOD:

Materials: Carbidopa is a gift sample of Aurobindopharma Ltd, Hydroxy propyl methyl cellulose is collected form Hi-media Chemicals Pvt. Ltd, Guargum is procured from Qualikems Fine ChemPvt.Ltd, Lactose, Magnesium stearate and talc are collected from finer chemicals.

Method of preparation:

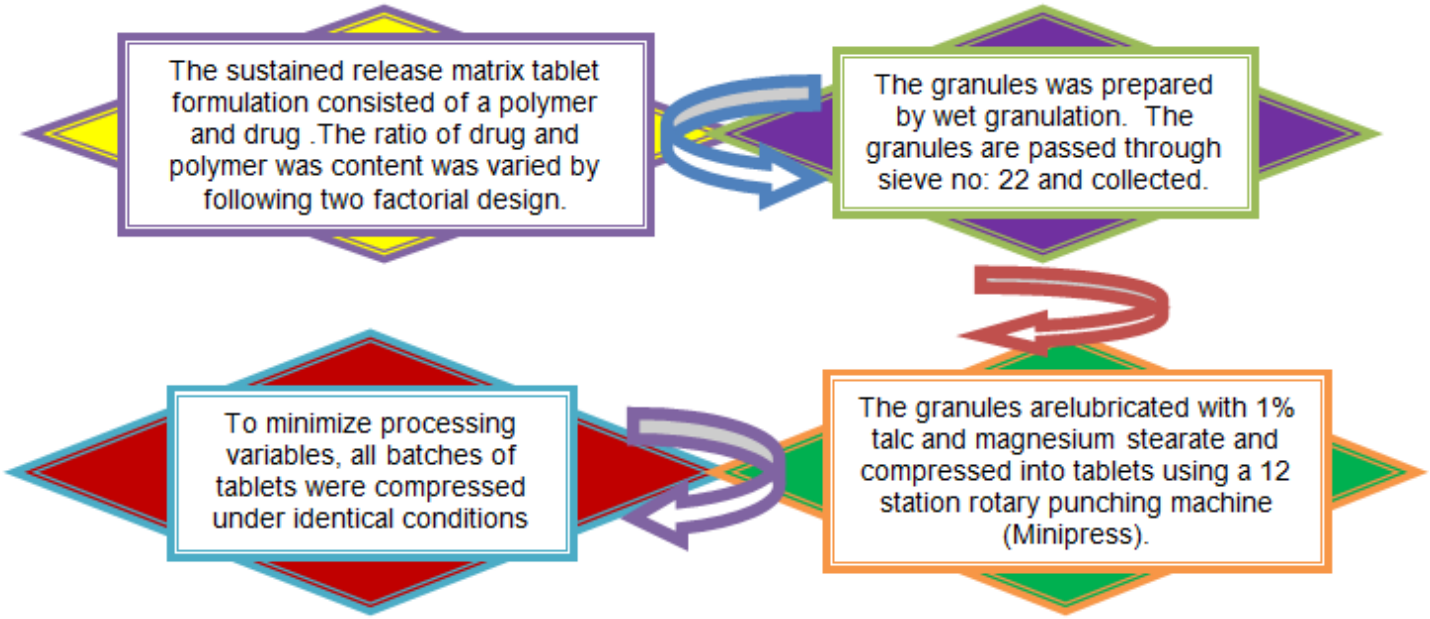

Figure 1: Preparation method

Table 1: Composition of sustained release matrix tablets

S. No	Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)
1	Carbidopa	100	100	100	100
2	HPMC K15M	25	25	25	25
3	Guar gum	12.5	12.5	6.25	6.25
4	Lactose	102.5	115	108.5	121.5
5	Magnesium stearate	5	5	5	5
6	Talc	5	5	5	5
Total Weight		250	250	250	250

RESULTS AND DISCUSSION:

Physical examination of tablets from each formulation found to be circular shape with no cracks.

Table 2: Micrometric properties of all formulations:

Parameter	F1	F2	F3	F4
Angle of repose	25	25.86	26	27.87
Bulk density (gm/ml)	0.60	0.612	0.520	0.841
Tapped density (gm/ml)	0.883	0.721	0.674	0.98
Compressibility index (%)	23	20	21	22

Thickness: Thickness of all tablets was found to be within the limit of + 5% of size of the tablet and was uniform in all the batches. The results are given in Table 3 .

Hardness: The measured hardness of the tablets of each formulation range between 4 to 5.0 Kg/cm. This ensures the good handling characteristics of all the formulations. The results are given in Table 3.

Weight variation: The average percentage weight variation for all the formulations was shown in Table 3. All the tablets passed weight variation test as the average percentage weight variation remained within the pharmacopoeial limits.

Friability: The percentage friability was less than 1% in all the formulation ensuring that the tablets were mechanically stable. The results are given in Table 3 .

Drug Content In Tablets: The amount of drug content in each tablet has been evaluated for all the four formulation. From this study the drug content in all the tablets was found to be within the specified limits (90% to 110%). This indicates that all the formulations of carbidopa were passing the drug content uniformity. The values are given in table 3.

Table 3: Physical properties of the tablets and Drug content of tablets:

Formulation code	Weight Uniformity (Mg)	Hardness (Kg/M$^{2)}$	Friability (%)± Sd	Drug Content Mg/Tab
F1	248±3.0	4±0.5	0.9±2.5	99±0.5
F2	249±3.0	4.2±0.3	o.89±2.6	100±0.3
F3	248±4.0	4.5±0.2	0.92±3.1	98±0.5
F4	250±2.0	4.1±0.2	0.95±2.5	99±0.4

IN-VITRO DISSOLUTION STUDY:

Dissolution test was carried out on 6 tablets from each formulation, using the USP apparatus II (paddle method, Pharma test, PTWS3, Germany) at 75 rpm. Dissolution medium for all formulations was 900 ml phosphate buffer pH 6.8 containing 0.1M Hcl buffer maintained at 37±0.5 °C. The drug release studies continued for 8 h and at certain time intervals, 5 ml samplesof the dissolution medium were withdrawn, centrifuged and assayed at 307 nm. After each sampling, an equal volume of fresh buffer solution, at the same temperature, was replaced (12).The in-vitro dissolution of all the 4 formulations was carried out using USP dissolution test apparatus and the results are given in following Table 4.

Table 4: Data of In-Vitro Drug Release Studies of controlled-release matrix tablets of Carbidopa

TIME (min)	% DRUG RELEASE			
	F1	F2	F3	F4
0	0	0	0	0
60	20.62	27.87	34.90	32.48
120	27.43	36.43	44.34	42.80
180	36.00	45.43	52.68	50.26
240	44.34	56.63	62.12	59.70
300	54.43	58.60	68.26	65.85
360	58.17	65.41	81.4	76.39

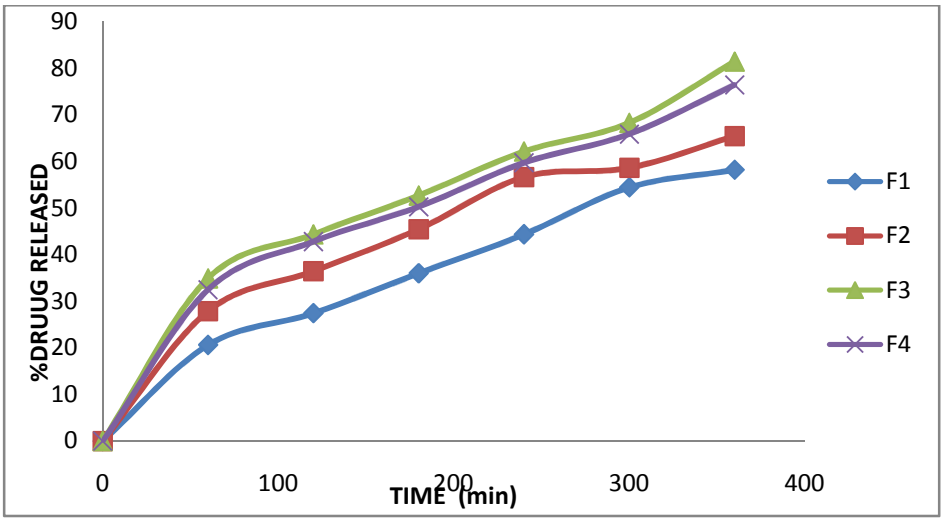

Figure 2: **Drug release profiles of various controlled release formulations of Carbidopa with Hydroxypropylmethyl cellulose and Guargum**

DRUG AND POLYMER COMPATIBILITY STUDIES

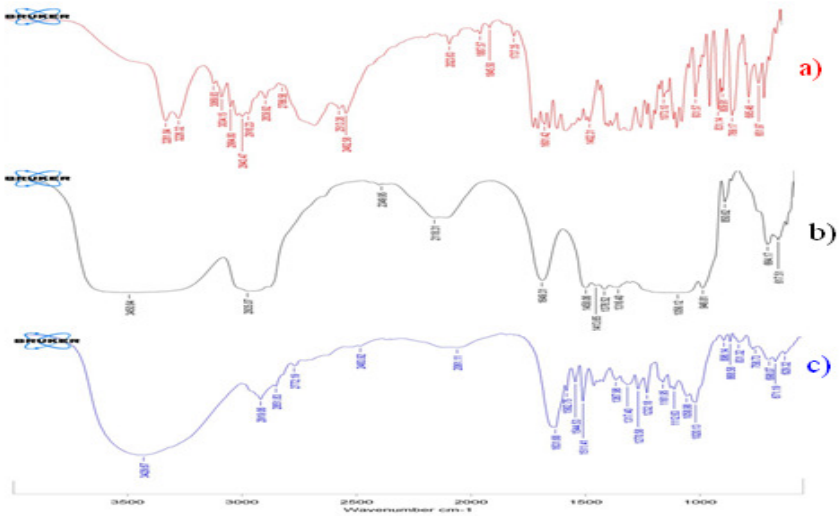

Figure 3:FTIR spectrum of a) Carbidopa, b) HPMC K15 and c) final formulation.

Table 5: Wave number for different functional groups in drug and formulation.

Functional group	Wave number range (cm^{-1})	Wavenumber (cm^{-1})		
		Drug	HPMC-K15	Formulation
O-H Stretching	3200 - 3700	3098	3402	3090
-O- Stretching	1000 - 1200	1000	1056	1003
N-H (2^o amine) stretching	1500 - 1700	1582	-	1586
H-N-H bending	1600 - 1650	1614	-	1655

FTIR studies show that there were no changes/negligible changes in wavenumbers of functional groups for Carbidopa. They remained same for drug and formulation also. This reveals that there is no change in functional group of drug in formulation .So there is no interaction between drug and excipients.

CONCLUSION:

The study was undertaken with the aim to Formulation and evaluation of Carbidopa controlled release matrix tablets using HPMC and guargum grade of polymers as retarding agents. From the above results and discussion, it is concluded that the formulation of controlled release tablets of Carbidopa containing HPMC ,guar gum and Lactose which are taken as ideal or optimized formulation of controlled release tablet for 6 hours release as it fulfills all the requirement of controlled release tablet. From the kinetic study it was known that F3 formulation showed highest release due to HPMC and Guargum retarding properties and study encourages further clinica ltrials and long term stability study on this formulation.

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