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Influence of *Momordica charantia* in physical properties and release profile of curcumin formulations

S.M. HABIBUR RAHMAN[1]*, CHUNGATH THOMAS TELNY[2] and S. KUPPUSAMY[3]

[1]Department of Pharmaceutics, PSG College of Pharmacy, peelamedu, Coimbatore (India)
[2]Department of Pharmaceutical Analysis, St. James College of Pharmacy, Chalakudy (India)
[3]Department of Pharmaceutics, Sri Ramakrishna Institute of Paramedical Sciences, Coimbatore (India)

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ABSTRACT

The goddess of curcumin gives color to life. Drug delivery approaches yet to be carried out to achieve the therapeutic benefit of phytoconstituent. Most of the herbal formulations emerging in the market are combination of phytomolecules[1]. Present study carried out to study the effect of *Momordica charantia* in curcumin formulation. Curcumin and *Momordica charantia* combination was widely used as anti-diabetic formulation. This combination is formulated as sustained release matrix tablets using HPMC and Ethyl cellulose by direct compression method. Formulated tablets were subjected to various *in vitro* evaluations; novel spectrophotometric method was developed and validated to quantify the *Momordica charantia* in the formulations.[2] All formulation showed acceptable pharmacotechnical properties with excellent flow properties, *in vitro* release studies suggest that incorporation of *Momordica charantia* in curcumin formulations has no significant influence in the release profile. To conclude, the *momordica charantia* can be incorporated in curcumin formulations for its synergistic activity, *in vivo* studies can be carried out to claim the therapeutic effectiveness of the formulations.

Key words: *Momordica charantia*, Curcumin.

INTRODUCTION

The goddess of curcumin gives color to life. The curcumin is a potent phytoconstituent with wide range of biological activity.[3] The poor solubility and photosensitive nature of curcumin makes it worthwhile to formulate as novel delivery system[4]. India has a rich history of using plants for medicinal applications. Traditional herbal remedies have led scientists to the development of numerous modern drugs. Formulation development for the herbal constituents yet to be established, most of the herbal formulation are existing as polyherbal formulation due to the unknown mechanism of the herbs. Curcumin and *Momordica charantia* is one such polyherbal formulation in practice for its hypoglycemic activity. The study has carried out to investigate the influence of *Momordica charantia* extract in curcumin dissolution profile.

MATERIAL AND METHODS

Momordica charantia is obtained from Himalaya health care Ltd, curcumin is obtained from Aldec pharma, German, HPMC and ethyl cellulose were procured from Loba chemie Pvt Ltd, and all other materials were of analytical grade.

Preformulation

Chemical and physical characterizations of drug substance are essential before the formulation development. Preformulation studies give the information needed to define the nature of the drug substances and provide a framework for the drug combination with pharmaceutical excipients in the fabrication of dosage form. The compatibility of the extracts with excipients was analyzed by FTIR and TLC.

Weighed amount of the extract (3mg) was mixed with 100 mg of Potassium bromide (dried at 40°-50°C), which was then compressed under 10-ton pressure in a hydraulic press to form a transparent pellet. Similarly, was prepared the pellets of individual polymers and that is combination with the extracts was prepared and scanned from 400-4000 cm^{-1} in FTIR spectrophotometer (JASCO).

TLC was done according to the earlier studies[5]

Analytical method development

500 mg of *Momordica charantia* dry extract was dissolved in water and made up to volume in a 100 ml volumetric flask to give 5 mg/ml concentration. 1 ml of stock solution was diluted to 100 ml using water to produce 50 µg/ml. Aliquots of samples 2,4,6,8 and 10 ml was transferred into 10 ml standard flasks and volume is made up to the mark with water to give a concentration 10,20,30,40 and 50 µg/ml. The absorbance of the above solutions was observed at 536 nm in UV-Vis spectrophotometer (shimadzu). Curcumin was estimated at 430nm in UV-Vis spectrophotometer (shimadzu)[6].

Preparation of tablet

Curcumin, *momordica charantia* and Micro Crystalline Cellulose, Dibasic Calcium Phosphate were triturated thoroughly in a glass mortar using a pestle, polymers were incorporated in the powder mix and finally magnesium stearate and talc were added as lubricant and glidant respectively. The prepared blend was compressed into tablets using single punch rotary tableting machine using 12 mm flat punch with constant compression force.

Drug polymer ratio

HPMC-10%, 15%, 30%: Ethyl Cellulose-2%, 3%, 6%

Evaluation -angle of repose

The static angle of repose was measured according to the fixed funnel and free standing cone method[7]. A funnel was clamped with its tip 2 cm above a graph paper placed on a flat horizontal surface. The powders were carefully poured through the funnel until the apex of the cone thus formed just reached the tip of the funnel. The mean diameters of the base of the powder cones were determined and the tangent of the angle of repose calculated using the equation:

Angle of repose = $\tan^{-1} h\backslash r$

Where, h is height of heap of powder and r is the radius of the base of heap of powder.

Densities

Bulk density and compressibility was measured by using standard procedures.[7,8]

Evaluation of sustained release tablets[7,8]

Pfizer hardness tester was used for measuring the hardness of the formulated Sustained release matrix tablets. The friability test was performed for all the formulated tablets.

Weight variation

The U.S.P. weight variation test was run by weighing 10 tablets and then the average weight was determined. All the 10 tablets were weighed individually and compared with the average weight, the percentage weight variation were calculated and reported.

Thickness

The thickness of the tablet was determined using a vernier caliper (Mitutoyo, New delhi, India) five tablets from each batch were used and average values were calculated.

Swellability

This was measured at the same time as the hydration capacity determination using the method of Okhamafe *et al.*[9]. The swelling index of the prepared tablets was evaluated for six tablets of each batch. These tablets were weighed and placed separately in pre-weighed basket made of stainless steel mesh. The total weight was recorded (W_1). This basket was placed in a plastic vessel containing pH 7.4 (phosphate buffer) and placed in an incubator at 37°C. At time intervals 0.5,1,2,3 and 4 hours excess buffer was carefully removed and the swollen tablets were weighed (W_2). The swelling index was determined from the formula Swelling Index = swollen weight (W_2-W_1) / Initial weight (W_1)

Dissolution

In vitro drug release was studied using USP I apparatus, with 900 ml of dissolution medium maintained at 37±1 C for 12h, at 100 rpm. 0.1N HCL (pH 1.2) was used as dissolution medium for the first 2 h, followed by pH 7.4 Phosphate buffer for further 10 h. 10ml sample was withdrawn after each hour, and was replaced by an equal volume of fresh dissolution medium of same pH. Collected samples were analyzed colorimetrically at 430nm, and cumulative percent drug release was calculated.

RESULTS

The sustained release tablets were formulated as per the batch specification in Table 1. All the formulations prepared with the addition of *Momordica charantia* showed acceptable pharmacotechnical properties with excellent flow properties and the results were shown in Table 2. The prepared tabkets were subjected to various quality control studies and the results are shown in Table 2a. The swellability of the tablets in relation to the time is shown in Fig 1. *In vitro* release profile of curcumin from the formulated sustained release matrix tablets were shown in Fig 2. Incorporation of ethyl cellulose was found to control the drug release. Higher concentration of hydrophilic and hydrophobic polymer combination can be used to achieve control release of *Momordica charantia* till 12 hrs.

DISCUSSION

The *Momordica charantia* is crystalline in nature and liable to adsorb moisture. Due to the crystalline nature it provides better flow properties. The addition of *Momordica charantia* is not having any significant influence in the rate of release of curcumin. The hydrophilic nature of the extract is not producing any retardation in the release of hydrophobic curcumin, so only the hydrophilic polymer concentration plays the significant role in achieving controlled release profile of curcumin. To achieve the control release of *Momordica charantia* in this polyherbal formulation is possible by increasing the concentration of hydrophobic

Table 1: Batch specification for different formulations containing Curcumin and *Momordica charantia*

Batch specification & polymer Ingredients	Curcumin & *Momordica charantia* in HPMC			Curcumin & *Momordica charantia* in HPMC combined with ethyl cellulose			
	CM1	CM2	CM3	CM4	CM5	CM6	CM7
Drug - polymer ratio	1:0.35	1:0.7	1:0.23	1:0.42	1:0.42	1:0.84	1:0.28
Curcumin	300	300	300	300	300	300	300
Momordica charantia	50	50	50	50	100	50	50
Microcrystalline Cellulose	112.5	60	130	101	77	39	123
Dicalcium phosphate	112.5	60	130	101	77	39	123
Magnesium stearate	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10
Hydroxypropylmethyl Cellulose	105	210	70	105	105	210	70
Ethyl cellulose	-	-	-	21	21	42	14
Total weight	700	700	700	700	700	700	700

polymer concentration. It's evident that a combination of hydrophilic and hydrophobic drugs can be made into sustained release tablets by optimizing the concentration of both kinds of polymers. From the available plethora of literatures the combination of *Momordica charantia* and curcumin showing better hypoglycemic conditions while compare to the individuals. By this study reports the combination can be made into sustained release formulation to achieve a better therapeutic response.

Table 2: Evaluation of powder blend

Formulation	Angle of repose (θ)	Loose bulk density (g/ml)	Tapped bulk density (g/ml)	Carr's index (%)
CM1	24.28	0.431	0.482	10.58
CM2	26.58	0.561	0.612	8.33
CM3	23.12	0.451	0.498	9.43
CM4	25.21	0.555	0.621	10.62
CM5	21.58	0.482	0.541	10.90
CM6CM7	27.5824.01	0.4810.476	0.5310.521	9.418.63

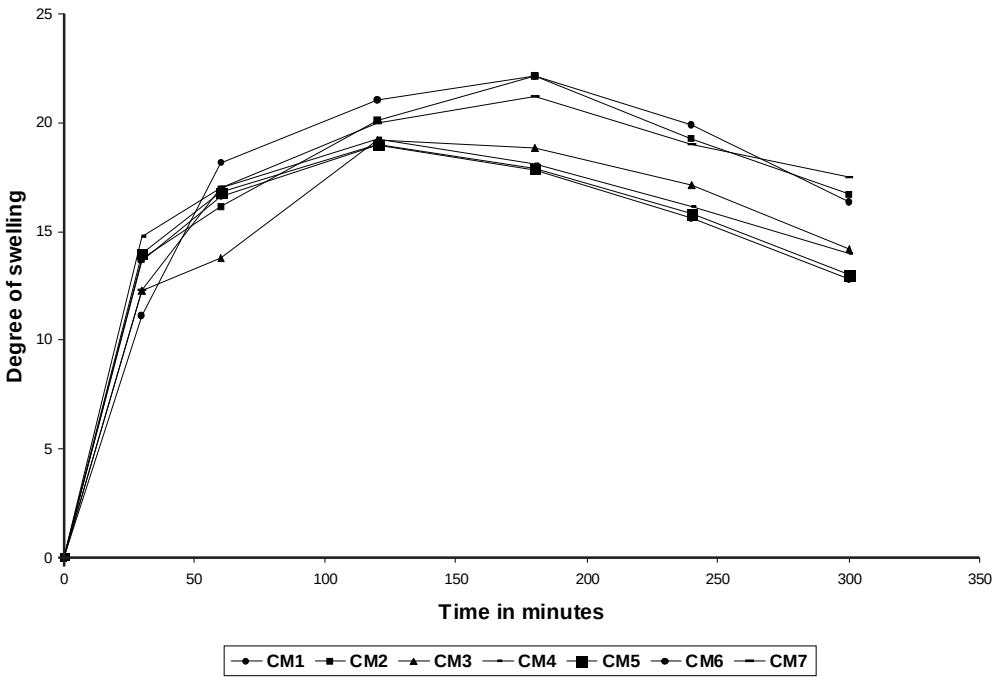

Fig. 1: Relationship between the time and the swelling index of the formulated sustained Release Matrix tablets

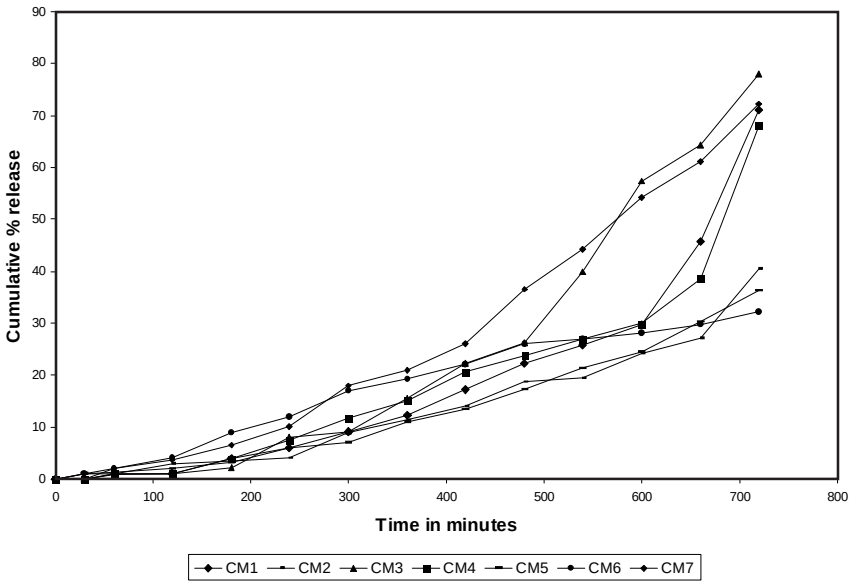

Fig. 2: *In vitro* dissolution profile for the formulated tablets containing curcumin and *Momordica charantia*

Table 2(a): Evaluation of sustained release matrix tablets

Formulation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight variation (%)
CM1	4	6.7	0.78	1.812
CM2	4	7.2	0.76	1.912
CM3	3.98	8.2	0.68	1.852
CM4	4.11	8.9	0.65	1.750
CM5	4.12	7.9	0.72	1.510
CM6	4	7.1	0.65	1.251
CM7	3.99	8.2	0.78	1.821

CONCLUSION

To conclude, the *Momordica charantia* can be included for the synergistic action with curcumin. The combination of HPMC and Ethyl cellulose combinations provides controlled release profile for both phytoconstituents. The characterization of *Momordica charantia* can be carried out and the pharmacokinetic studies will help in claiming the therapeutic response of the phytomolecules.

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