# FORMULATION AND IN-VITRO EVALUATION OF DEXTRIN MATRIX TABLET OF IBUPROFEN FOR COLON SPECIFIC DRUG DELIVERY

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**ABSTRACT**
The objective of the present study is to develop colon targeted drug delivery system by using dextrin (polysaccharide) as a carrier for ibuprofen. Matrix tablets containing various excipients and dextrin were prepared by wet granulation technique using different binder systems. The matrix tablets were evaluated by different IPQC tests, content uniformity and in vitro drug release study. Drug release profile was evaluated in simulated gastric, intestinal fluid and simulated colonic fluid. Best formulation was decided on the basis drug release profile in simulated gastric and intestinal fluid. The matrix tablet containing dextrin as a carrier and ethyl cellulose as binder was found to be suitable for targeting ibuprofen for local action in the colon as compare to other matrix tablets containing different binders because of fewer amounts (8-11%) of drug release in the simulated gastric and intestinal fluid. Matrix tablets containing dextrin released 95-98% of ibuprofen in simulated colonic fluid with 4% human fecal matter solution. Tablets containing dextrin showed no change in physical appearance and dissolution profile upon storage at 40$^{o}$C/75% relative humidity for three months. The results of *in-vitro* study indicate that matrix tablets containing dextrin as carrier and ethyl cellulose as binder are most suitable to deliver the drug specifically in colonic region as compare to matrix tablets of dextrin with other binder systems.

**Keywords**: Ibuprofen, matrix tablet, dextrin, colon specific drug delivery.

## INTRODUCTION

Since from last decade a novel oral colon-specific drug delivery system (CDDS) has been developing as one of the site-specific drug delivery systems. This delivery system, by means of combination of one or more controlled release mechanisms, hardly releases drug in the upper part of the gastrointestinal (GI) tract, but rapidly releases drug in the colon following oral administration (Kinget *et al*., 1998; Watts *et al*., 1997; Yang *et al*., 2002). CDDS is convenient for treating localized colonic diseases, i.e. ulcerative colitis, Crohn's disease and constipation *etc.*, CDDS, also selectively deliver drug to the colon, but not to the upper GI tract (Kinget *et al*., 1998). Colon is referred to as the optimal absorption site for protein and polypeptide after oral administration, because of the existence of relatively low proteolytic enzyme activities and quite long transit time in the colon. CDDS would be advantageous when a delay in absorption is desirable from a therapeutically point of view, as for the treatment of diseases that have peak symptoms in the early morning and that exhibit circadian rhythms, such as nocturnal asthma, angina and rheumatoid arthritis (Kinget *et al*., 1998; Halsas *et al*., 2001; Halsas *et al*., 1999).

The aim of this study was to explore the feasibility of the colonic microorganism to develop CDDS by using ibuprofen as model drug.

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Polysaccharides, the polymer of monosaccharide retains their integrity because they are resistant to the digestive action of gastrointestinal enzymes. The matrices of polysaccharides are assumed to remain intact in the physiological environment of stomach and small intestine but once they reach in the colon, they are acted upon by the bacterial polysaccharides and results in the degradation of the matrices. A large number of polysaccharides such as amylose, guar gum, pectin, chitosan, inulin, cyclodextrins, chondroitin sulphate, dextrans, dextrin and locust bean gum have been investigated for their use in colon targeted drug delivery systems. The most important fact in the development of polysaccharide derivatives for colon targeted drug delivery is the selection of a suitable biodegradable polysaccharide. As these polysaccharides are usually soluble in water, they must be made water insoluble by cross linking or hydrophobic derivatisation.Very important is an optimal proportional of the hydrophobic and hydrophilic parts respectively and the number of free hydroxy groups in the polymeric molecule (Halsas *et al*., 2001 and Zou, 2001).

## MATERIAL AND METHODS

Ibuprofen IP- Shree Swami Samartha Ayurvedic Pharmaceuticals, Jalgaon (MS) as gift sample. Ethyl Cellulose, MCC, Dextrin, Sucrose, Sodium CMC, Magnesium Stearate-LOBA Chem, Lobachem Pvt., Ltd., P.O. Box No.6139, Mumbai 400005, India having LR

**Table 1**: Composition of different dextrin matrix tablets of ibuprofen

| Sr. No. | Name of Ingredient | Grades | Quantity/tablet (mg) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Formulation codes | | | | | | | | |
| | | | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| 01 | Ibuprofen | | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 02 | Dextrin | (LR) | 050 | 075 | 100 | 050 | 075 | 100 | 050 | 075 | 100 |
| 03 | Micro crystalline Cellulose | (LR) | 340 | 310 | 280 | 340 | 310 | 280 | 340 | 310 | 280 |
| 04 | Sodium CMC (10% aq. solution) | (LR) | 005 | 010 | 015 | - | - | - | - | - | - |
| 05 | Sucrose (70% aq. solution) | (LR) | - | - | - | 005 | 010 | 015 | - | - | - |
| 06 | Ethyl cellulose (10% alcoholic solution) | (LR) | - | - | - | - | - | - | 005 | 010 | 015 |
| 07 | Magnesium stearate | (LR) | 005 | 005 | 005 | 005 | 005 | 005 | 005 | 005 | 005 |
| | Total weight of Tablet | | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 |

**Table 2**: I.P.Q.C. Parameters of different dextrin matrix tablets of ibuprofen

| Formulation Codes | IPQC Parameters | | | | |
|---|---|---|---|---|---|
| | Average Weight of Tablets (mg) | Average Diameter of Tablets(cm) | Average Hardness of Tablets (kg/cm$^2$) | Friability of Tablets (%) | Average Thickness of Tablet (mm) |
| F1 | 502 | 01 | 5.0 | 0.33 | 3.1 |
| F2 | 501 | 01 | 4.5 | 0.31 | 3.0 |
| F3 | 497 | 01 | 5.5 | 0.31 | 3.1 |
| F4 | 498 | 01 | 5.0 | 0.29 | 3.1 |
| F5 | 501 | 01 | 5.5 | 0.28 | 3.2 |
| F6 | 498 | 01 | 4.5 | 0.24 | 3.1 |
| F7 | 499 | 01 | 5.5 | 0.30 | 3.0 |
| F8 | 502 | 01 | 4.0 | 0.28 | 3.2 |
| F9 | 492 | 01 | 6.5 | 0.29 | 3.0 |

grade. All other chemicals used for assay were of analytical grade.

***Preparation of granules***

Granules were prepared by using wet granulation method by using different binder systems. Details of granulation are given in following table I (Lachman *et al*., 1990).

***Preparation of tablets***

Initially granules were treated with lubricants like talc and magnesium stearate. Tablets were prepared by compressing the lubricated granules on rotary tablet compression machine by using 10mm SC (Shallow concave) die and punch set. Details of compression parameters are given in following table I (Lachman *et al*., 1990).

***Study of in process quality control parameters of tablets***

Tablets were evaluated during compression for different IPQC parameters like Weight, Hardness, Thickness, Diameter, and Friability.

Thickness and diameter of the tablet were measured using caliper scale. Hardness was evaluated manually by using Monsanto hardness tester. Friability test was performed at speed of 25 rpm with tablets dropping from height of six inches with each revolution. After the test, the tablets were dedusted and reweighed. Results are shown in table 2 (Indian Pharmacopoeia, 1996).

***Drug content uniformity test for tablets***

Ibuprofen tablets were analyzed by Indian Pharmacopoeia method and results are as shown in table 3.

Twenty tablets were weighed and powdered. Crushed powder of tablets equivalent to 0.15gm was taken. 50 ml of 0.1M sodium hydroxide was added to the powder and diluted with 100 ml of water. Resultant solution was exposed to shaking for 15 min. sufficient water was added to same to produce 200 ml of solution. The solution was mixed and filtered. 10 ml of filtrate was diluted with water up to 100 ml. 10 ml of 0.1M sodium hydroxide was added to 10 ml of resulting solution. This solution was diluted with water up to 100 ml and mixed. Finally absorbance of the resulting solution was measured at the maximum at about 257 nm. Content of ibuprofen was calculated taking 715 as the value of A (1%, 1 cm) at the maximum at about at about 257 nm. (Indian Pharmacopoeia, 1996).

**Table 3**: Results of drug content uniformity test of different dextrin matrix tablets of ibuprofen (I.P. specification (95%-105%).

| Sr. No. | Formulation Codes | Assay ( % Drug Content) |
|---|---|---|
| 1 | F1 | 101.62 |
| 2 | F2 | 98.03 |
| 3 | F3 | 97.49 |
| 4 | F4 | 99.92 |
| 5 | F5 | 98.50 |
| 6 | F6 | 98.03 |
| 7 | F7 | 104.63 |
| 8 | F8 | 95.68 |
| 9 | F9 | 99.13 |

***In vitro drug release study***

Test was carried out using USP apparatus II (paddle) and the medium was Simulated gastric fluid, Simulated intestinal fluid and simulated colonic fluid. Quantity of dissolution medium was 900 mL. The speed of paddle was 50 rpm and temperature of dissolution medium was 37.5°C. One tablet was placed in the dissolution medium and apparatus was run. At intervals of 2, 5, 8, 12, 16, 20 and 24 hours, 5 mL aliquots were withdrawn and replacement was made each time with 5 mL of fresh dissolution medium. Each 5 mL sample was filtered through Whatman filter paper no. 41 and diluted up to 50 ml with respective dissolution medium. Then absorbance was measured at 249 nm (USP 27).

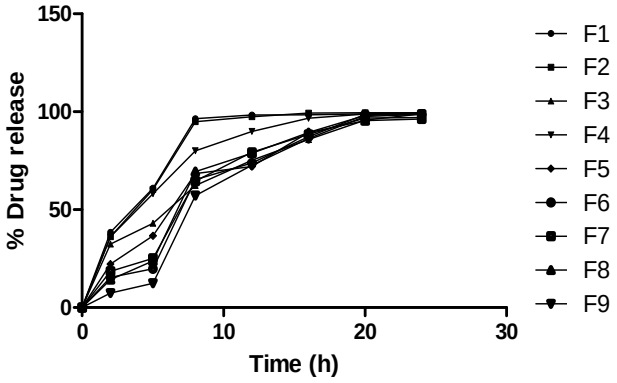


**Fig**. % Drug release pattern of different dextrin matrix tablets of ibuprofen.

***Stability study***

Best formulation was (F9) exposed to three months stability study at 40°C/75% RH. These samples then again evaluated for drug release study (Momin *et al.*, 2004 and Krishnaiah *et al.*, 2001).

## RESULTS AND DISCUSSION

Granules were prepared successfully by using wet granulation method and Tablets were prepared by

**Table 4**: Dissolution behavior of different dextrin matrix tablets of ibuprofen

| Dissolution Media | Time (Hrs.) | Cumulative % Drug Release* | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Formulation code | | | | | | | | | |
| | | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | Stability sample of F9 |
| Simulated Gastric Fluid | 02 | 38.40 | 36.24 | 32.42 | 36.20 | 22.18 | 15.42 | 18.62 | 14.30 | 07.39 | 08.36 |
| Simulated Intestinal fluid | 05 | 60.92 | 60.37 | 43.10 | 58.17 | 36.70 | 19.82 | 25.17 | 23.86 | 12.47 | 13.41 |
| Simulated Colonic Fluid | 08 | 96.46 | 94.92 | 62.34 | 80.12 | 68.42 | 65.34 | 64.59 | 69.48 | 57.16 | 56.07 |
| | 12 | 98.37 | 97.46 | 75.24 | 89.94 | 72.12 | 73.80 | 79.37 | 78.80 | 72.69 | 70.16 |
| | 16 | 98.46 | 99.32 | 85.80 | 96.67 | 89.38 | 87.13 | 88.40 | 89.36 | 86.32 | 82.30 |
| | 20 | 98.89 | 99.39 | 95.70 | 98.82 | 98.10 | 98.56 | 96.76 | 95.44 | 97.50 | 96.45 |
| | 24 | 98.92 | 99.46 | 98.97 | 99.40 | 99.24 | 98.84 | 97.08 | 96.27 | 98.69 | 99.06 |

*Figures of % drug release are mean of triplicate study.

compressing the lubricated granules on rotary tablet compression machine. Tablets were evaluated as per I.P. 96 guidelines. The hardness, percent friability and average thickness were found to be in the range of 4.0 to 5.5 kg/cm$^2$, 0.24 % to 0.33 %, 3.0 to 3.2 mm respectively. Tablets showed 95.68 to 104.63 % of the labeled amount of ibuprofen, indicating uniformity in drug content as per I.P. specification (95%-105%). All formulations were complying with the I.P. specifications.

Resulted tablets were evaluated for drug release by using USP dissolution apparatus II. Assay of tablet shows that tablets are of required purity and matches the I.P. specification. Drug release studies shows that F9 shows good release behavior in colon and restricts release in stomach and intestine as compare to F1–F8. This study confirms that dextrin can act as good carrier in the form of matrix tablet for ibuprofen to deliver it in colon specifically by using ethyl cellulose as binder.

Stability study of formulation No.F9 confirms that tablets are stable and there was no significant change in Hardness, Friability, Drug content and Dissolution profile of F9.

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