ISSN: 2321-3760

Research Article

International Journal of Current Trends in Pharmaceutical Research

IJCTPR, 2014, Vol. 2(5): 628-633

www.pharmaresearchlibrary.com/ijctpr

Preparation and Evaluation of Physical properties Ibuprofen matrix tablet using *Tamarand indica* as colon targeted drug

Prashant Patil[1*], S.N.Sriharsha[1], Yashwant Kumar.D[1], K.S.S.N. Neelima[2]

[1]*Pacific College of Pharmacy, Pacific University (PAHER), Udaipur, India*

[2]*SARC- (Scientific and Applied Research Centre) – Hyderabad*

Received: 09 July 2014, Accepted: 18 August 2014, Published Online: 15 September 2014

Abstract

The present study was undertaken to assess the potential of Tamarind seed polysaccharide (TSP) to act as a biodegradable carrier for colon specific drug delivery. Hence an attempt was made to develop matrix tablet based formulation using TSP which protects the drug in upper GIT and release the major amount of drug in colon due to degradation by bacterial enzymes. . The matrix tablets were prepared by dry granulation technique containing different concentrations (20% mg to 120% mg Quantity per each matrix tablet) of TSP using Ibuprofen as a model drug. The matrix tablets were evaluated for different quality control tests, content uniformity and *in-vitro* drug release study. Drug release studies were carried out in 0.1M HCl, pH 6.8 Sorensen phosphate buffer (SPB) and pH 5.9 phosphate buffer saline without rat caecal content. The drug release studies were carried out for 21 hours since the usual colonic transit time is 20−30 hours. Samples, 1ml, were taken at different time intervals and volume was made up to 10 ml with SPB, filtered and absorbance was measured at 221 nm. The prepared Ibuprofen matrix tablet using various proportion of *Tamarind indica* gum were evaluated for drug release profile for Colon Targeted Drug Delivery System. The per cent drug release in pH 6.8 SPB was more than 0.1M HCl. The result showed that, the matrix formulation F4 released almost the entire quantity of the drug at the end of 24 h dissolution study. It appears from these results that F4 could target ibuprofen to colon.

Keywords: Colon specific drug delivery, Tamarind seed polysaccharide, Matrix tablets, Biodegradable carrier, Enzyme induction

Contents

***Corresponding author**
Prashant Patil
Pacific College of Pharmacy,
Pacific University (PAHER), Udaipur
Manuscript ID: IJCTPR2235

PAPER-QR CODE

1. Introduction

In the recent years, considerable attention has been focused on the development of controlled drug delivery systems for the sake of convenience and ambulatory patient compliance, which is a problem normally, associated with some class of drugs such as NSAIDs, anti-hypertensive, anti-asthmatic and antipyretic drugs. Among all the methods, matrix dissolution controlled using swellable hydrophilic gums have been extensively investigated [1]. Polysaccharides like xanthan gum, scleroglucan, and gaur gum are some of the natural polysaccharides which have been evaluated in hydrophilic matrix for drug delivery system. Although tamarind seed polysaccharide (TSP) is used as an ingredient in food material and in pharmaceuticals has not been evaluated as hydrophilic drug delivery system. TSP is a galactoxyloglucan isolated from seed kernel of *Tamarindus indica*.

It possesses properties like high viscosity, broad pH tolerance and adhesively. This led to its application as stabilizer, thickener, gelling agent and binder in food and pharmaceutical industries. In addition to these other important properties of TSP have been identified recently. They include non-carcinogenicity, biocompatibility, high drug holding capacity and high thermal stability. This led to its application as excipient in hydrophilic drug delivery system [2]. Natural polymers have advantages over synthetic and semi-synthetic polymers like low cost, natural origin, less side effects, locally available and better patient tolerance. Since TSP is an important excipient, the present study designed to elucidate the solubility characteristics and dissolution behavior of TSP for water insoluble drugs [3].

The colon specific drug delivery is valuable in the topical treatment of colonic disorders such as irritable bowel syndrome, Cronh's disease and Ulcerative colitis and colon carcinomas. The delivery of drugs to colon is also useful for systemic absorption of drugs especially proteins and peptides which are degraded in upper GIT [4]. Some other examples of usefulness of colonic drug delivery in systemic absorption are antiasthamatics which are targeted to colon for the treatment of nocturnal asthama and antidiabetics like insulin which is degraded by the enzymes present in the upper gastrointestinal tract. The enzymatic activities associated with the microflora of the colon can be used as a tool for colon specific drug delivery. In addition the colon has a longer retention time and appears to be highly responsive to agents that enhance the absorption of poorly absorbed drugs. A colonic drug delivery system could be of absolute value where a delay in systemic absorption is therapeutically desirable, especially in the case of diseases which are affected b y Circardian rythems [5]

Ulcerative colitis is currently treated with anti-inflammatory medications such as sulfasalazine [6]. Enemas and suppositories are not effective for extensive proximal ulcerative colitis. In addition traditional oral dosage forms do not deliver drugs significantly to large intestine. To reduce their adverse effects, these agents should be targeted to the colon for the treatment of inflammatory bowel diseases by modified release oral formulations [7]. The colon specific drug delivery is required to protect the drug during its transit through upper GIT and allow its release in the colon. The large bacterial population present in the colon is a unique feature that allows the site specific drug delivery using polysaccharides. A number of carriers have been investigated by many coworkers. Guargum [3, 4], Pectin and its salts, amylose , amylose-ethocel films, chitosan and dextrin [9] have been studied for digestion by colonic bacteria for colon specific drug delivery.

The present study aims at utilization of Tamarind seed polysaccharide (TSP) [10] as a carrier for colon specific drug delivery. Ibuprofen, a derivative of propionic acid is nonsteroidal anti- inflammatory drug used as a model drug in this study is found to be effective in rheumatic diseases such as osteoarthritis, rheumatoid arthritis, juvenile chronic arthritis and acute arthritis. Ibuprofen is also useful in periarticular and musculoskeletal indications for analgesia in bursitis, tenditis, fibrosis, tenosynovitis, lumbago, neck pain and myalgia of all types. It is also indicated in infectious diseases for analgesic, antipyretic and anti-inflammatory purpose [11].

2. Materials and Methods

Materials:

Ibuprofen was received as a gift sample from Universal Medicaments Pvt. Ltd, Nagpur, India. Tamarind seed powder (TSP) was procured from Lucid Group, India. Tragacanth powder (Sigma,UK), sodium carboxy methyl cellulose (Nacmc), Theophylline (Wako, Japan). Ibuprofen was gratis sample from Zim Laboratories, Nagpur. Sodium chloride, microcrystalline cellulose was obtained from Signet Chemical Corporation, Mumbai. All the chemicals and reagents used in the study were of analytical grade.

Methods:

Collection and authentification plant part:

The *Tamarindus indica* Linn seeds were collected from different region of Maharashtra in the month of November 2012. The plant part was authenticated by department of botany, Rajasthan University, Jaipur. A voucher specimen

was deposit in the herbarium, university of Rajasthan, Jaipur.

Isolation of *Tamarindus indica* gum*:*

The crushed seeds of *Tamarindus indica* were soaked in water for 24 h, boiled for 1 h, and kept aside for 2 h for the release of gum into water. The soaked seeds were taken and squeezed in a muslin bag to remove marc from the filtrate. Then, to the filtrate, equal quantity of absolute ethyl alcohol was added to precipitate the gum. The gum was separated by filtration. The marc was not discarded but it was sent for multiple extractions with decreasing quantity of extracting solvent, i.e., water with the increase of number of extractions. The isolation was continued until the material was free of gum. The separated gum was dried in hot air oven at temperature 40 C. The dried gum was powdered and stored in airtight containers at room temperature.

3. Formulation and evaluation

Formulation and evaluation of ibuprofen matrix tablet containing tamarand indica

1. Preparation of granules:

Tamarand indica gum powder was sieved and mixed with ibuprofen and MCC and sieved together to ensure complete mixing. The blend was granulated using 10% w/v polyvinylpyrrolidone (PVP) in isopropyl alcohol as binder. The wet mass was passed through and dried at 40 °C for 6 hours.

2. Preparation of tablet:

Six tablet formulations were prepared (Table 1). The amount of ibuprofen in each case was 100 mg. The dried granules were passed through a sieved and mixed with magnesium stearate and talc. The lubricated granules were compressed using 8 mm round, standard biconcave punches on a pilot press tablet machine (Chamunda Pharma Machinery Pvt. Ltd.). The average weight of tablet was kept between 198−209 mg.

3. Evaluation of Physical properties of matrix tablets:

3.1 Weight variation:

Twenty tablets from each composition were weighed individually and average weight was calculated. Then the individual tablet weights were compared to the average tablet weight.

3.2 Thickness testing:

The thickness of the matrix tablets was determined using screw gauge, and the results are expressed as mean values of 10 determinations.

3.3 Friability:

Ten tablets were weighed and placed in the rotating disc of Roche friabilator. The apparatus was operated for four minutes at 25 rpm, deducted and weighed again. The percent of friability was calculated based on weight loss after the test.

3.4 Hardness:

The tablet was placed between the two anvils of Monsanto hardness tester and increasing amount of force was applied. The reading was directly read on the marked scale till a pressure required to break tablet was recorded.

3.5 *In Vitro* Drug Release

Drug release studies were carried out in 0.1M HCl, pH 6.8 Sorensen phosphate buffer and pH 5.9 phosphate buffer saline without rat caecal content. The matrix ibuprofen tablets were evaluated for their integrity in the physiological environmental of stomach and the small intestine under condition mimicking mouth to colon transit. The studies were carried out using a USP dissolution test apparatus I at 100 rpm and 37 °C. Each tablet was placed in baskets of apparatus and tested for 2 hours in 900 ml 0.1M HCl as the average gastric emptying time is about 2 hours. The dissolution medium was replaced with 900 ml pH 6.8 Sorensen phosphate buffer for 3 hours as the average small intestinal transit time is about 3 hours. At the end of the time periods i.e. 2 h and 3 h, samples each of 1 ml were taken separately, suitable diluted and analyzed for ibuprofen at 221 nm.

The studies simulating the drug release in colon were carried out in USP dissolution test apparatus I at 100 rpm and 37 °C with slight modification. A beaker of capacity 500 ml containing 200 ml of pH 5.9 phosphate buffer saline as dissolution medium was kept in water bath of dissolution test apparatus. The experiment was carried out with the continuous CO2 supply into beakers. The drug release studies were carried out for 21 hours since the usual colonic transit time is 20−30 hours. Samples, 1ml, were taken at different time intervals and volume was made up to 10 ml with Sorensen phosphate buffer, filtered and absorbance was measured at 221 nm.

3. Results and Discussion

Evaluation of Physical properties of matrix tablets

As shown in table 3, the compressed tablets were tested for weight variation, thickness hardness, friability and drug content. All the weights were within ±7.5% deviation range and passed the weight variation test according to IP 1996. The hardness of the tablets was found to be about 3.0 kg/cm2. Friability index is a

measure of integrity of the material, which is a function of cohesiveness. It is an indication of endurance of material during various operations like packaging, transportation and handling. The generally agreed upper limit for friability is 1%. The friability of the tablets was found within the desirable range 0.4-1% and hence the tablets passed the friability test. The tablets were assayed and the drug content was found to be in the range 95.0 - 105%. Hence the tablets complied with IP standards.

Drug release Studies

Studies in absence of rat caecal contents

The ability of *Tamarind indica* gum polysaccharides to retain integrity of the tablets in the physiological environment of stomach and small intestine, and prevent complete drug release was assessed by conducting drug release studies in 0.1M HCl and 6.8 Sorensen phosphate buffer for 2 and 3 hours respectively, according to conditions mimicking mouth to colon transit (Table 4). Results of the drug release studies in 0.1M HCl for 2h and pH 6.8 SPB for 3 hours from ibuprofen matrix tablets indicate tamarind indica gum polysaccharide is capable of protecting the drug at higher concentration (40%, 50% and 60 %w/w) as the cumulative per cent drug release after 5 hours were 16.19±0.170, 11.34±0.096 and 9.18±0.154 respectively. The drug release was relatively higher at lower concentration i.e. (10, 20 and 30%). As the carrier concentration increases from 10 − 60% w/w, there was progressive decrease in drug release. Considering drug release in pH 5.9 Sorensen phosphate buffer and protection provided by the carrier in simulated upper GI fluids and 40,50 and 60% w/w carrier concentration were selected for further studies in rate caecal contents and in galactomannase enzyme, as at these concentration the drug release was less, indicating higher resistance to drug release

Table 1: Different tablet composion of Ibuprofen matrix tablet containing *Tamarand indica* gum

Ingredient	**Quantity per each matrix tablet (mg)**					
	F1	F2	F3	F4	F5	F6
Ibuprofen	75	75	75	75	75	75
Tamarand indica Gum	20	40	60	80	100	120
Microcrystalline cellulose	101	81	61	41	21	1
Magnesium stearate	2	2	2	2	2	2
Talc	2	2	2	2	2	2
Total (mg)	200	200	200	200	200	200

Table 2: Physical properties of granules

Carrier Concentration (%w/w)	**Angle of repose (q°)**	**Bulk density Pb (g/cm3)**	**Tapped density Pt (g/cm3)**	**% compressibility**
10	20.0	0.911	0.96	5
20	23.8 0.	819	0.88	7.
30	23.8	0.820	0.89	8.
40	22.1	0.877	0.95	8.
50	21.0	0.872	0.96	10.
60	21.3	0.812	0.91	11.

Table 3: Physical properties of matrix tablets

S.No	**Formulation code**	**Hardness (kg/cm2)**	**Thickness (mm)**	**Weight variation(mg)**	**Friability (%)**	**Content Uniformity (%)**
1	F1	3.0±0.04	2.75±0.04	198.34±7.23	0.79	96.5
2	F2	2.9±0.09	2.75±0.06	198.38±8.56	0.91	95.75
3	F3	3.0±0.00	2.70±0.06	197.25±6.23	0.82	99.10
4	F4	2.8±0.00	2.80±0.02	202.63±9.56	0.65	101.40
5	F5	2.9±0.06	2.80±0.00	202.42±8.25	0.55	100.2
6	F6	3.0±0.00	2.74±0.08	197.15±9.56	0.43	98.50

Table 4: Cumulative mean percent drug release (Mean± SD; n=3) After 2 hours in 0.1M HCl and 3 hours in pH 6.8 Sorensen phosphate buffer from matrix tablets.

S.No	Formulation code	Concentration of carriers (% w/w of tablet weight)	Mean per cent drug release (Mean±SD, n=3)		Cumulative mean percent drug release (Mean ±SD; n=3) 0.1M HCl (After 5 hr)
			0.1M HCl (2 hours)	pH 6.8 SPB (3 hours)	
1	F1	10	9.52±0.577	32.6±0.254	42.±0.415
2	F2	20	9.55±0.517	23.88±0.463	33.43±0.490
3	F3	30	7.39±0.151	16.07±0.340	23.46±0.245
4	F4	40	6.57±0.00	9.62±0.340	16.19±0.170
5	F5	50	3.50±0.08	7.84±0.112	11.34±0.096
6	F6	60	3.44±0.08	5.74±0.228	9.18±0.154

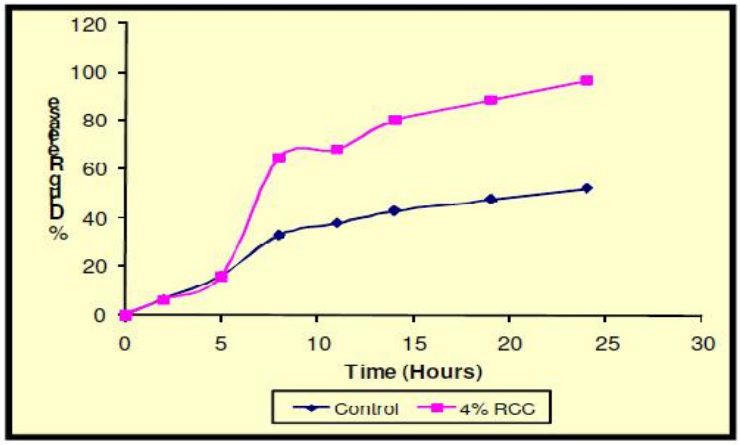

Figure 1: Release profile of matrix tablet containing 40 % W/W carrier Percent drug release (Mean ± SD; n=3) of 10 to 60%

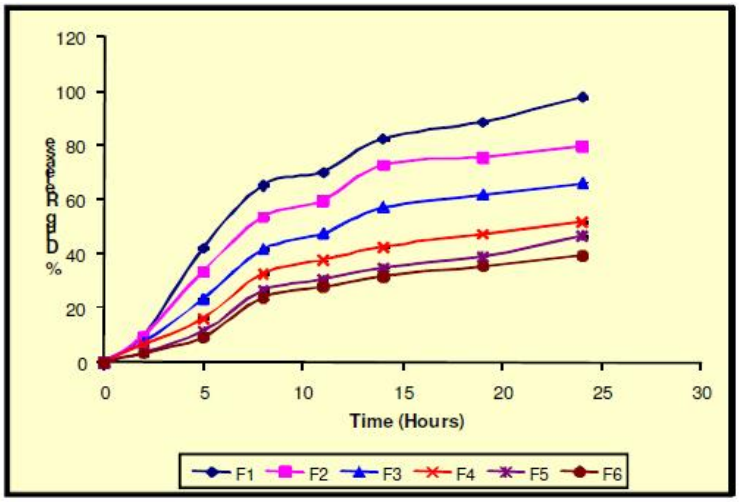

Figure 2: Carrier concentration from matrix tablets.

6. Conclusion

The results obtained in this study established for the first time, the fundamental characteristics of the gum obtained from the fresh seeds of *Tamarand indica*. The gum performed better than sodium carboxy methyl cellulose at 30% w/w as a sustained release excipient. It was also found to be pH sensitive and may therefore be useful in intestinal drug delivery. The results indicate that the cumulative mean percent drug release decrease with increased carrier concentration. The percent of ibuprofen released from F4 at the end of 24 h was found to be 96.27%. Whereas the control studies, it was found to be 52.04%. The Results shows that F4 formulation might be acted upon by colonic bacteria within 5-6h of entering the colon and release most of the

drug in the colon. Hence, the matrix formulation F4 released almost the entire quantity of the drug at the end of 24 h dissolution study. It appears from these results that F4 could target ibuprofen to colon.

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