International Journal of Advanced Multidisciplinary Research
ISSN: 2393-8870
www.ijarm.com
(A Peer Reviewed, Referred, Indexed and Open Access Journal)
DOI: 10.22192/ijamr Volume 8, Issue 7 -2021

Review Article

DOI: http://dx.doi.org/10.22192/ijamr.2021.08.07.001

Formulation and evaluation of colon targeted matrix tablets of Ibuprofen: A Review

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Keywords

Ibuprofen, Ulcerative colitis, FT-IR, physicochemical parameters.

Abstract

Chronic condition is a Ulcerative colitis is of inflammation and ulcers in colon and rectum, the present study was to developed Ibuprofen colon targeted matrix tablet for effective treatment of Ulcerative colitis. Formulation of Ibuprofen matrix tablets was prepare by using different polymers such as Eudragit S-100 and Ethyl cellulose (as carriers) in different ratios. Ibuprofen tablet were prepared by direct compression method. Based on FT-IR study drug and excipient compatibility was checked and confirmed the nil interactions. The prepared tablets were coated with an enteric polymer and were evaluated for the physicochemical parameters such as hardness, thickness, content uniformity, drug content and *in vitro*-drug release studies. Among the six formulation F6 showed better drug release 98.51% of Ibuprofen. The stability study was also conducted, the results showed there is no significant changes of drug content and other parameter, which make a clearance of Ibuprofen matrix tablet formulation.

Introduction

The effective and safe therapy for colonic disorders, colon specific drug delivery is necessary. The colon targeted tablets drug release and absorption should not occur in the stomach as well as the small intestine, and neither the bioactive agent should be degraded in either of the dissolution sites but only released and absorbed once the system reaches the colon. Nowadays colon specific drug delivery is challenging task to pharmaceutical technologist. The colon is to be a suitable absorption site for peptides and protein drugs for the reasons of less diversity and Intensity of digestive enzymes[1].Comparative proteolytic activity of colon mucosa is much less than that observed in the small intestine, thus Colon targeted drug delivery system. protects peptide drugs from hydrolysis, and enzymatic degradation in duodenum and jejunum, and eventually releases the drug into ileum or colon which leads to greater systemic bioavailability[2]. The concentration of drug reaching the colon depends on formulation factors, the extent of retrograde spreading and the retention time[3]. Coating of the drugs with pH-sensitive polymers provides simple approach for colon-specific drug delivery[4]. The medicament should be absorbed once the reaches the colon. To reach the colon has a long residence time 72 hours and having high water content it favors absorption of poorly absorbed drug molecule may have an improved bioavailability. Colon targeted drug delivery system has the advantage of

- Controlled / Sustained release thus reduce dosing frequency
- Targeted delivery of drug to achieve high concentration in treatment of disease of distal gut
- Deliver drug to that region that is less hostile metabolically, drug which is acid and enzyme labile such as proteins [5].

A glance of colonic absorption and disease:

The absorption capacity of colon is very high which is attributed to the colon transit time, which can be as long as 20-35 hours, hence it is ideally suited for absorption. The absorption is influenced by the transport of water, electrolytes and ammonia across the mucus and it is more in the proximal colon than the distal colon. Drug molecules pass from the apical to basolateral surface of epithelial cells by Passing through colonocytes (trans cellular transport), or Passing between adjacent colonocytes (para cellular transport)

Inflammatory bowel disease:

Inflammatory bowel disease (IBD) is a group of inflammatory conditions of the colon and small intestine. Crohn's disease and ulcerative colitis are the principal types of inflammatory bowel disease. It affect the small intestine and large intestine, it can also affect the mouth, esophagus, stomach and the anus whereas ulcerative colitis primarily affects the colon and the rectum[6].

Ulcerative colitis:

Ulcerative colitis is an idiopathic, chronic inflammatory disorder of the colonic mucosa, which starts in the rectum and generally extends proximally in a continuous manner through part of or the entire colon however, some patients with proctitis or left-sided colitis might have a caecal patch of inflammation. Bloody diarrhoea is the characteristic symptom of the disease. Ulcerative colitis is a nonspecific inflammatory bowel disease of unknown etiology that effects the mucosa of the colon and rectum. The treatment of ulcerative colitis depends on the amount of the large bowel affected and the severity of the inflammation. Ulcerative colitis most often begins gradually and can become worse over time. Symptoms can be mild to severe. The goal of care is to keep people in remission long term[7].

Materials and Methods

Materials and source

Ibuprofen was obtained as a gift sample from Fourrts India Laboratory, Eudragit S100, Eudragit FS 30D-Vikram Thermo (India) Ltd, Ethyl cellulose - Jalan cellulose. Co, Lactose (DCL 21) - Cabot sanmar, Talc- Abishek organics. Magnesium stearate - Amishi Drugs & Chemical, & Co. Tri Ethyl Citrate- Chemtrec –International Ltd, all the above excipients and other chemicals used in these formulations are of analytical grade.

Method of matrix tablet preparation

The formula was designed as 450 mg tablet. There was six formulas (F1 to F6) ware developed. The various ratios of polymers and other additives in the formula ware mentioned in table 1.

Table .1: Formula of Ibuprofen Matrix Tablets

Sr. No.	Ingredients	Quantity of ingredients (mg/tab)					
		F1	F2	F3	F4	F5	F6
1	Ibuprofen	250	250	250	250	250	250
2	Eudragit S-100	80	60	50	35	20	14
3	Ethyl cellulose	60	55	40	25	15	10
4	Lactose (DCL 21)	50	75	100	130	154	165
5	Talc	5	5	5	5	5	5
6	Magnesium stearate	5	5	5	5	6	6
Total weight (mg)	450	450	450	450	450	450	450

Preformulation studies:

The basic purpose of the preformulation study was to provide a rational basis of the formulation and maximize the chances of formulation success and thus optimizing drug product quality and performance[8].

Evaluation of Active pharmaceutical ingredient:

The evaluation of ibuprofen was done according to Indian Pharmacopoeia standard.

Physical character Description

It is the initial evaluation in preformulation studies, which assess the colour, solubility, melting point and moisture content.

Solubility

Aqueous solubility is an important physicochemical property of drug substance, which determines its systemic absorption and in turns its therapeutic efficacy. As per the solubility specifications mentioned in table no.2. the sample is dried under specified conditions. Loss on drying of Ibuprofen was measured by using moisture balance. Approximately 2gm of Ibuprofen was placed into a plate of moisture balance and set the temperature to 45°C. Measured the moisture content of drug in percentage.

Table .2: Solubility Specifications

Descriptive terms	Approximate volume of solvent in milliliters per gram of solute
Very soluble	Less than 1
Freely soluble	From 1 to 10
Soluble	From 10 to 30
Sparingly soluble	From 30 to 100
Slightly soluble	From 100 to 1000
Very slightly soluble	From 1000 to 10,000
Practically insoluble	More than 10,000

Flow Properties (Angle of Repose)

To assess the flow property powder by angle of repose funnel method. Accurately weighed powder blend was taken in a beaker, it was allowed to flow through the funnel freely on the surface of the paper to form a cone shaped pile. The diameter of the cone (d) and the height (h) of the pile was noted. From the diameter, radius (r) was calculated. The angle of repose (θ) was calculated using the following formula. Θ = tan – 1(h/r)[9]

Bulk density

Bulk density is an indicator of compaction. It is defined as the weight of powder occupying a unit volume and is expressed in g/ml. Bulk density depends on the particle size distribution. It is expressed in g/ml. An accurately weighed quantity of granules was transferred into a 50 ml measuring cylinder. The unsettled apparent volume, to the nearest graduated unit occupied by the powder was measured. Bulk density was determined using the formula.10 ρbulk = m/Vo Where, ρbulk = Bulk density; m = Mass of the blend Vo = Untapped Volume [10]

Tapped density:

Tapped density was measured by mechanically tapping of measuring cylinder containing a powder sample. After observing the initial volume, the cylinder is mechanically tapped, and volume readings are taken until little further volume change is observed. The measuring cylinder containing a weighed quantity of powder (after measurement of bulk density) was subjected to 500 taps in tapped density tester (Electro Lab USP II). The tapped density was calculated by using the formula. ρt = m/Vt Where, ρt = Tapped density m = Mass of the granules Vt = Final tapped volume.

Table. 4. Carr's compressibility index

S. No.	Compressibility index (%)	Flow characters
1	< 10	Excellent
2	11-15	Good
3	16-20	Fair
4	21-25	Passable
5	26-31	Poor
6	32-37	Very poor
7	>38	Extremely poor

Measurement of powder compressibility Carr's compressibility index:

The Carr index or Carr's Compressibility index is an indication of the compressibility of a powder. The Carr index is frequently used as an indication of the flow ability of a powder. Ibuprofen cars was calculated by using the formula.[11] The compressibility description index was shown in table number 4. CI = ρt – ρ bulk / ρt × 100 Where, CI = Compressibility index ρbulk = Bulk density

ρt = Tapped density

Table .5 Hausner's ratio as an indication of powder flow

S. No.	Hausner's ratio	Type of flow
1	1.0 –1.11	Excellent
2	1.12 – 1.18	Good
3	1.19 – 1.25	Fair
4	1.26 – 1.34	Passable
5	1.35 – 1.45	Poor
6	1.46 - 1.59	Very poor
7	>1.60	Extremely poor

Hausner's ratio:

Hausner's ratio is simply the tapped density divided by the bulk density. Compressibility and Hausner ratio parameters are influenced by variables such as particle size and shape and cohesivity, since they essentially reflect the impact of tapping on the particle packing. Hausner's ratio description are mentioned in table no. 5It was calculated using the formula.12 Hausner's Ratio = ρt / ρbulk[12]

Where, ρbulk = Bulk density
ρt = Tapped density

Preparation of Enteric Coating solution:

A required quantity of Eudragit FS 30 D was weighed accurately and stirred. Meanwhile Triethylcitrate was added to it, purified talc were triturated separately in a mortar and added to the solution and stirred well. Finally the volume were make up to required quantity with purified water. Filtered the above solution with #100 mesh. Weight built up calculation for enteric coating: [6 %] 450(Tablet weight) X 6 % (Coating) =27 g The weight of enteric coated tablet = (450 + 27) = 477 477mg. Coating was done in following specification, speed of revolution 10-12 rpm, spray rate 1.5 – 2 ml per minute, dry air temperature 500 ± 50 C / 30 minutes, coating time 4 hour and bed temperature 300 -400

Hardness:

Tablets require a certain amount of strength or hardness to withstand mechanical shocks of handling in manufacture, packaging, and shipping. Tablet hardness has been defined as, the force required to break a tablet in a diametric compression test. Tablet hardness of all the formulations was measured using a Monsanto hardness tester.[13]

Thickness:

Tablet thickness is an important parameter to be controlled to facilitate packaging. Tablet thickness, at constant compressive load, varies with changes in die fill, with particle size distribution and packing of the particle mix being compressed; whereas at constant die fill, thickness varies with variations in compressive load.

Tablet thickness must be controlled within a ±5% variation of a standard value.12 Thickness of all the formulations was measured using a digital vernier 76 tandar.

Friability:

Friability is a measure of the resistance of the tablet to abrasion. The measure is useful to determine the ability of the tablet to withstand abrasion during handling, coating, packing and transport. Friability was measured by using Roche friabilator, this device subjects the tablets to the combined effects of abrasion and shock by utilizing a plastic chamber that rotates at 25 rpm, dropping the tablets form a height of 6 inches with each revolution. Twenty tablets were weighed accurately and placed in the friabilator and was operated for 100 revolutions or 4 minutes. The tablets were then de dusted and weighed. The weight loss of 0.5 to 1% is considered as acceptable limits for conventional uncoated tablets. The weight loss was calculated using the formula.[14]

Disintegration Test:

USP disintegration test specifies that one tablet is added to each of the six tubes in the USP disintegration apparatus. The apparatus is operated without disks, using simulated gastric fluid (pH 1.2) at 370C for 2 hrs. The tablets are then removed and must show no evidence of disintegration, cracking or softening. Disks are then added and the apparatus is operated using simulated intestinal fluid (pH 7.4) at 370C for a period of time limit specified in the monograph.[15]

Weight Variation Test:

Twenty tablets were selected randomly and weighed individually. Calculate average weight and compare the individual tablet weight to the average. Not more than two of the individual weights deviate from the average weight by more than the percentage shown in and none deviate by more than twice the percentage.

Results and Discussion

Preformulation studies: The preformulation study results were shows Ibuprofen and excipients have a adaptability for make Colon targeted matrix tablets the results are tabulated in following tables.

Physical characteristics of Ibuprofen

The colour, solubility, melting point and moisture content of the Ibuprofen was found to be within the range of the monograph,

Flow property-angle of repose

The angle of repose of Ibuprofen was found to be 380.56′± 0.690. Hence the drug belongs to fair flow and requires glidants to improve the flow property. The results

Bulk density and tapped density of Ibuprofen

The average bulk density and tapped density was found to be within a range 0.453 ± 0.01 and 0.614± 0.003 g/ml respectively.

Conclusion

The Ibuprofen matrix tablets were successfully formulated by direct compression method using the selected excipient quantities. The formulated tablets were evaluated for both pre-compression and post-compression parameters as per requirements of standards. And the results were complied with the pharmacopoeia specification. The formulated Ibuprofen matrix tablets were coated with enteric polymer Eudragit FS 30D by pan coating method.

From among the entire batches, formulation F6 showed 98.51% drug release at 24 hrs. Since it provide greater protection to the core under acidic condition while at the same time show the fastest drug release under intestinal pH. So the trial F6 was considered as best formulation. From the results obtained, it can be concluded that formulation F6 containing enteric coated matrix tablet of Ibuprofen would be a promising formulation to achieve the purpose which treat inflammatory bowel diseases (ulcerative colitis) without any gastric irritation or ulcers, which is useful for patients having pre history of ulcerative colitis.

Acknowledgments

We would like thank to our Principal Dr. Prakash H. Patil and Guid Anup Akarte, And thanks to K.V.P.S's Institute of Pharmaceutical Education Boradi, for providing laboratory facilities, internet, books, journals, and to done this work.

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Website: www.ijarm.com

Subject: Pharmaceutical Sciences

Quick Response Code

DOI:10.22192/ijamr.2021.08.07.001

How to cite this article:
Amit Kharde Kalpesh More, Anup Akarte, Pankaj Chaudhari, Prakash Patil. (2021). Formulation and evaluation of colon targeted matrix tablets of Ibuprofen: A Review. Int. J. Adv. Multidiscip. Res. 8(7): 1-8.
DOI: http://dx.doi.org/10.22192/ijamr.2021.08.07.001