IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

A MOUTH DISSOLVING TABLET : ACECLOFENAC

SRI SAI COLLEGE OF PHARMACY ,BADHANI PATHANKOT

Muskan , Manjit kaur ,Nikhil choudary , Dr . Rajesh gupta

Keywords : Aceclofenac powder, dry granulation, geriatric, mouth-dissolving tablet, pediatric, wet granulation

Abstract

Aceclofenac has been shown to have potent analgesic and anti-inflammatory activities similar to indomethacin and diclofenac, and due to its preferential Cox-2 blockade, it has a better safety than conventional Non steroidal anti-inflammatory drug (NSAIDs) with respect to adverse effect on gastrointestinal and cardiovascular systems. Aceclofenac is superior from other NSAIDs as it has selectivity for Cox-2, a beneficial Cox inhibitor is well tolerated, has better Gastrointestinal (GI) tolerability and improved cardiovascular safety when compared with other selective Cox-2 inhibitor [1,2]. To provide the patient with the most convenient mode of administration, there is need to develop a fast-disintegrating dosage form, particularly one that disintegrates and dissolves/disperses in saliva and can be administered without water, anywhere, any time. Such tablets are also known as mouth melt tablets or melt in mouth tablets.

INTRODUCTION

Many patients find it difficult to swallow tablets and hard gelatin capsules and thus do not comply with the prescription which results in noncompliance and ineffective therapy. Recent advances in novel drug delivery systems aim to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration to achieve better patient compliance. Rapidly disintegrating tablet are appreciated by significant segment of the population, particularly pediatric, geriatric, unconscious, and bed-ridden patients who have difficulty swallowing conventional tablet and capsule.[3,4]

To overcome this, dispersible tablets and fast-disintegrating tablets have been developed. Most commonly used methods to prepare these tablets are freeze drying/lyophilization, tablet moulding, and direct compression methods. Lyophilized tablets show a porous structure, which causes very quick penetration

of saliva into the pores when placed in oral cavity, but it has disadvantage of high cost production process.

Conventional aceclofenac tablet available in the market are not suitable for acute pain and inflammatory conditions where quick onset of action of drug is required. This is because of poor patient compliance, particularly by the geriatric and pediatrics patient who experience difficulty in swallowing, and by those who are bed ridden or who are traveling and do not have an easy access to water. Aceclofenac is superior from other NSAIDs as it has selectivity for Cox-2, a beneficial Cox inhibitor, well-tolerated, better GI tolerability, and improved cardiovascular safety than other selective Cox-2 inhibitors. It also shows increased matrix component synthesis and protection of chondrocytes against apoptosis. Aceclofenac has a faster and more potent effect than the other NSAIDs. Aceclofenac has a faster and more potent effect than the other NSAIDs. It efficiently interferes with neutrophils adhesion to endothelium and this effect may represent an additional relevant mechanism in its anti-inflammatory activity[4]. Aceclofenac has an outstanding anti-inflammatory profile, involving a classical inhibition of prostaglandins E_2, a decrease in the expression of several cytokines including interleukin and tumor necrosis factor. It also inhibits activated oxygen species production and influences cell adhesion. It is mainly used for osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, dental pain, postoperative pain, post-traumatic pain, low back pain, and gynecological pain. Thus, it can be concluded that aceclofenac may be a better option for the management of pain. The drug is official in British Pharmacopoeia. Aceclofenac is practically insoluble in water, and peak blood level reaches between 1 to 3 hours after oral administration. These tablets were evaluated for their friability, hardness, wetting time, and disintegration time.

Aceclofenac has been shown to have potent analgesic and anti-inflammatory activities similar to indomethacin and diclofenac, and due to its preferential Cox-2 blockade, it has a better safety than conventional Non steroidal anti-inflammatory drug (NSAIDs) with respect to adverse effect on gastrointestinal and cardiovascular systems. Aceclofenac is superior from other NSAIDs as it has selectivity for Cox-2, a beneficial Cox inhibitor is well tolerated, has better Gastrointestinal (GI) tolerability and improved cardiovascular safety when compared with other selective Cox-2 inhibitor. To provide the patient with the most convenient mode of administration, there is need to develop a fast-disintegrating dosage form, particularly one that disintegrates and dissolves/disperses in saliva

The rapidly disintegrating tablets in oral cavity can be swallowed with a small amount of water or saliva. The tablet manufactured by any of the above mention methods are composed of drug and other excipients which disintegrate in small amount of water or saliva in the oral cavity within 30 seconds. Hence, an attempt was made to improve the dissolution of aceclofenac through the formulation of mouth-dissolving tablets with appropriate mechanical strength, which would disintegrate in oral cavity, in less than 30 seconds, and would provide an immediate relief from pain due to its faster dissolution in gastrointestinal tract.[5,6]

As aceclofenac tablets plays a major role in the relieving of the pain which may occur in the joints ,that is arthritis osteoarthritis,ankylosis etc

PREPARATION AND EVALUATION

The wet granulation and direct compression technique were selected for developing a novel mouth-dissolving formulation

1 . In wet granulation, all materials were passed through a 40 mesh. Aceclofenaxc , Avicel PH 102 which is micro crystalline cellulose powder along with sodium lauryl sulfate were mixed properly

2 . Alcoholic solution of PVPK30 was added to mixture in quantity just enough to bind the mass; granulation was done by passing the wet mass through a 14 mess.

3 Granules were dried at 60°C for 30 minutes, then pass through 20 mesh, and granules were used for further processing

4 . Granules were mixed with granular fraction of the lubricant/glidant and require proportion of fines particles of at least 10 percent in the requirement. The resulting mass then compressed into tablet using single punch tablet machine.

5. Then the preparation of tablet which is acting as pain reliever melts in the mouth as of its flow properties .[7,8]

EVALUATION OF TABLETS (pharma times 2004)

Tablets are the solid unit dosage forms containing a medicament which shows therapeutic effect in the body as the tablet is made up of mixture of medicament and excipients compressed or moulded into solid .

GENERAL APPEARANCE

The general appearance of a tablet, its virtual identity and overall elegance is essential for consumer acceptance ,for control of lot to lot uniformity

Appearance of a tablet involved the measurements of a tablets to Exiplicate size ,shape, color , odor , taste and surface texture.

ORGANOLEPTIC PROPERTIES

Many pharmaceutical tablets use color as vital means of rapid identification and consumer acceptance . The color of a product must be uniform within a single tablets

SIZE AND SHAPE: it is to be measured by micrometer and sliding caliper scale

tablet thickness should be controlled within _+5% variation of the standard value.

HARDNESS FRIABLITY TESTING

Tablet requires a certain amount of strength , or hardness and resistance to friablity , to withstand mechanical shocks of handling in manufacture , packing and shipping

hardness is also termed as the checker of tablet crushing strength .

Tablet hardness tester are like for eg. Pfizer tester , Erweka tester , strong cobb tester .

FRIABLITY

The friabilty test is official in USP but not in BP and IP

friablity tester is known as the **roche friabilator .** tablet hardness is not an absolute indicator of strength since some formulations ,when compressed into very hard tablets.

PROCEDURE includes

1. preweighted tablet sample placed in friabilator
2. operated 100 revolutions (25rpm for 4 minutes)
3. Dropping tablet a distance 6 inch tablets are then dusted and reweighted conventional compressed tablet that loss less than 0.5 to 1 % of their weight are generally acceptable .

WEIGHT VARIATION

The weight of the tablet being made is routinely measured to help ensure that a tablet contains the proper amount of drug

as per indian pharmacopoeia IP weight 20 tablet selected

at random and determine the average weight not more than 2 of the individual weight deviate from the average

weight by more than the percentage deviation shown

Average wt. table	Max % of difference
130 or less	10 %
130 -345	7.5 %
more than 345	5 %

CONTENT UNIFORMITY

The potency of tablets is expressed in the terms of grams , milligrams ,or micrograms of drug per tablet and is given as the label strength of the product

Determine the amount of active ingredient by the method in the assay .the result lies within the range for content of active ingredient stated in the monograph .

This test is applicable to tablets that contain less than 10 mg or less than 10% w/w of the active ingredient .it is not applicable to tablets containing multivitamin and trace element .

As per IP

Ten tablets are taken at random ,there content of active ingredient is determine in each of 10 tablets and the average value is calculated

1 The sample passes the test is not more than one of the individual value is the outside the limit of 85 to 115% of the average value .

2 If two or three of the individual tablets are outside limits 85 to 115 % of the average value and none is the outside limit about 75 to 125%

3 The test is repeated using another 20 tablets

WETTING TIME

A circular tissue paper of 10cm diameter were placed in a Petri dish having an internal diameter of 10 cm. 10 ml of water containing methylene blue (10% w/w) was added to the Petri dish. The tablet was carefully placed in the centre of the Petri dish and the time taken for the water to reach the upper surface of the tablets was known as wetting time

DISSOLUTION TEST APPARATUS

Dissolution is the process by which a solid solute enters a solution.

Pharmaceutically , it may be defined as the amount of drug substance that goes into solution per unit time under standardized

Conditions of liquid / solid interface , temperature and solvent composition.

This test apparatus is used to conclude the solid which may get entered to the solution.

It is carried out in

1 USP dissolution apparatus type 1 (basket type)

2 USP dissolution apparatus type 11 (paddle type)

In general , a single tablet is placed in a small wire mesh basket fastened to the bottom of the shaft connected to a variable speed motor .

The basket is immersed in the dissolution medium (as specified in the monograph) contained in a flask . The flask is maintained at constant temperature of 37 degree celsius by a constant temperature bath.

DISINTEGRATION TEST APPARATUS

it is the time required for the tablet to break into particles the disintegration test is a measure only of the time required under a given set of conditions for a group of tablets to disintegrates into particles .

Liquids used in disintegration

Water , simulated gastric fluid ph = 1.2 HCL

USP methods for uncoated tablets:

Start the disintegration test on 6 tablets

If one or the two tablets from the 6 tablets fail disintegrate completely within 30 minutes repeat the same test on the another tablet

not less then 16 tablets disintegrates completely within time

If more then two tablets from the 18 fail to disintegrate , the batch must be rejected.

For coated tablets:

To remove or dissolve the coat ,immerse the tablet in distilled water for 5 minutes

Put the tablet in the apparatus in water or hcl for 30 minutes at 37 degree celsius according to the USP .if not disintegrated ,put in intestinal fluid

If one or two tablets fail to disintegrate ,repeat on 12 tablets

If more then 2 not disintegrated the batch is rejected.

CONCLUSION

A Tablet in Capsule device containing Aceclofenac tablet for Pain Management with Gastro protection was formulated. Rationale of combining a NSAID and a prostaglandin analogue was well justified and the design of drug delivery system was made simple by encapsulating two different tablets (Aceclofenac in single capsule and it offers advantage in terms of GI protection, Patient Compliance and Chronotherapeutics.[11,12]

• Aceclofenac extended release tablet 200mg was formulated using various grades of hydrophilic polymer such as HPMC E50, HPMC K100 LV CR, HPMC K4M CR and HPMC K15M CR as release retardant to prolong the release for 12 hr .[16]

• Misoprostol Immediate release tablet 200mcg was formulated using Crospovidone as superdisintegrant at 2%, 3% and 4%.

• Formulation characteristics such as precompression and postcompression studies of the developed formulations were carried out separately as per standard procedures.

• The tablets were found to be within the limits with respect to uniformity of weight, hardness, thickness, diameter, friability and drug content.

• In vitro dissolution studies for both the tablets were conducted separately.

• Aceclofenac ER formulation A8 was optimized based on the ideal release upto 12 hr

• The optimized Aceclofenac formulation followed Zero order release kinetics

• Based on the disintegration time Misoprostol IR formulation M3 was optimized

• The optimized formulations of Aceclofenac A8 and Misoprostol M3 were used for
filling in size 0 elongated capsules.

• The stability studies under accelerated conditions of 40± 2°C /75±5% RH was found to be satisfactory .

Acknowledgement

I would like to express my special thanks of gratitude to my project teacher “Mrs . Manjit kaur “ for their able guidance and support in completing my project review . I also want to express my gratitude to our principal sir Mr Rajesh Gupta to evaluate good prospectus of their students and to guide them for their bright future.

REFERENCES

1 Swarbrick and Jc boylan eds encyclopedia of pharmaceutical technology vol 12 regarding the introduction of aceclofenac tablet .the study of texture shape and pharmacological action.

2 Banker gs & Rhodes c.t Modern pharmaceutics variations in the potency of the dose of the drug administered to the body of the human being .

3 Lachman et al 2009 tylor and franchies preffered to look after the science after the pharmacological action towards the drug dose the book was written in a perfect order to imply the dosage administered in the patients body .

4 Vinayak V Ranade, Mannfred A Hollinger. Drug Delivery Systems. 2nd ed. Boca Raton: CRC press; 2004. p. 2. Regarding the drug delievery system action to the body .

5 Chien Yie W (ed.). Novel drug delivery systems. 2nd ed. New York: Marcel Dekker, Inc;1992: p. 139. Have initiated with the aceclofenac uses as well as the research based on the benificial outcome of the preparation in the tablet.

6 Jayesh Parmar, Manish Rane. Tablet formulation design and manufacture: oral Immediate release application. Pharma Times 2009;41(4). Evaluations and procedures.

7 Gilbert S Banker, Christopher T Rhodes (ed.). Modern Pharmaceutics. 4th ed. New York: Marcel Dekker, Inc.; 2002.

8 Eugene F Fiese, Timothy A Hagen. Preformulation. In: Leon Lachman, Herbert A Lieberman, Joseph L Kanig. (eds.) The theory and practice of industrial pharmacy. 3rd ed. Mumbai: Varghese Publishing House; 1987. p.171, 293-294,374.

9 Nain NK. Pharmaceutical Product development. New Delhi: CBS Publisher and distributors; 2006. p. 426

10 Capscanada [Online]. Available from : http://www.capscanada.com/assets/technical%20specifications%20gelatin%20cc%20w%20lq [Accessed 10th October 2011]

11 Vyas SP, Roop K Khar. Controlled Drug Delivery concept and advances. New Delhi: Vallabh Prakashan; 2002. p. 1-9.m

12 Robinson JR. Sustained Release Drug Delivery Systems. In: Remington. The Science and Practice of Pharmacy.19th ed. San Francisco: Mack Publishing Company;1995. p.1081- 1082.

13 Jayanthi B, Manna PK, Madhusudhan S, Mohanta GP, Manavalan R. Per oral extended release products - An overview. Journal of Applied Pharmaceutical Science 2011;1(2):50- 55.

14 SunilKamboj. Matrix tablet an important tool for oral controlled release dosage forms. Pharmainfo.net [Online] Available from: www.pharmainfo.net/reviews/matrix-tablets-important-tool-oral-controlled-release-dosage-forms [Accessed 15th October 2011]

15 Sandip B Tiwari, Ali R Rajabi-siahboomi. Modulation of drug release from hydrophilic systems

16 Melanie Dumarey, Hakan Wikstrom, Magnus Fransson, Anders Sparen, Pirjo Tajarobi, Mats Josefson et al. Combining experimental design and orthogonal projections to latent structures to study the influence of microcrystalline cellulose properties on roll compaction. International Journal of Pharmaceutics 2011;416:110– 119.