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Research Article

Anti- Arthritic Activity Of Sustained Release Tablet Of Indomethacine

Manisha Karsh*, Rajesh Kumar Chandra, Sudhir Kathane, Shruti Rathore

LCIT School of Pharmacy, Bilaspur Chhattisgrah-495220, India

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ABSTRACT

In the present investigation an attempt has been made to study the formulation and evaluation of matrix tablets of Indomethacin using mucilage of hibiscus rosa-sinensis as a release retardant. The mucilage was extracted from the leaves of hibiscus rosa-sinensis using acetone. The matrix tablet were formulated using different concentration (0.15, 0.3 and 0.45) of hibiscus mucilage. The developed formulation of tablets were evaluated for pre-compression and post-compression parameters. The result of precompression parameters like bulk density, tap density, carr's index and Hausner's, ratio were found to be within the limits indicating good flow properties of the granules. Swelling index reveals that with increasing mucilage concentration there is increased swelling showing 68% for F3 at the end of 5 hours where as for F1 and F2 it was around 58.3% and 66.66% respectively. In-vitro drug release for F3 formulation was found to be 62.86% at the end of 8 hours. With increase mucilage concentration the drug release from the matrix tablets got retarded. In-vitro drug release data obtained were fitted to various release models access the possible mechanism of the drug release. All the formulation showed matrix (Higuchi Matrix) as a best fit model and the release mechanism was found to be Fickian Diffussion. The matrix tablets of Indomethacin formulated by using Hibiscus mucilage as a release retardant could be employed for retardant drug release. One of the most important (NSAID) non-steroidal anti-inflammatroy drug containing the indol core is represented by the indomethacin. This highly relevant compound has been used for the last 50 years with excellent pharmacological results. Arthritis is most prevalent disorder and Indomethacin choice of drug for arthritis. Oral route is most preffered route of the drug administration and tablets are more convenient dosage form.

INTRODUCTION

Introduction of matrix tablets as sustained release has given a new breakthrough for novel drug delivery in field of pharmaceutical technology. Sustained release (SR) drug delivery systems are developed to modulate the release of drug, in order to achieve specific clinical objectives that cannot be attained with conventional dosage forms. Possible therapeutic benefits of a properly designed SR dosage form include low cost, simple

***Corresponding Author:** Manisha Karsh
Address: *LCIT School of Pharmacy, Bilaspur Chhattisgarh -495220, India*
Email : karshmanisha3502@gmail.com

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processing, improved efficacy, reduced adverse events, flexibility in terms of the range of release profiles attainable, increased convenience and patient compliance. Arthritis is a term often used to mean any disorder that affects joint. Symptoms generally include joint pain and stiffness. Different types of arthritis exists (i) rheumatoid arthritis (ii) osteoarthritis, each with different causes including wear and tear, infections and underlying diseases.

Control Drug Delivery is that type of system which release the medicaments from the dosage form at a predetermined specified rate for locally or systemically for a specified period of time. It maintains constant drug level in the blood target tissue usually by releasing the drug in a zero order pattern. Controlled release, prolonged action, sustained release, extended release, depot dosage forms are terms used to identify these drug delivery systems that are designed to achieve prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of single dose.

TYPES OF ARTHRITIES

There are more than 100 different types of arthritis. Some of the most common types include:

a **Osteoarthritis (OA)** is a type of degenerative joint disease that results from breakdown of joint cartilage and underlying bone. It is believed to be the fourth leading cause of disability in the world, affecting 1 in 7 adults in the United States alone. The most common symptoms are joint pain and stiffness.

b **Rheumatoid arthritis (RA**) is a long-term autoimmune disorder that primarily affects joints. It typically results in warm, swollen, and painful joints. Pain and stiffness often worsen following rest. Most commonly, the wrist and hands are involved, with the same joints typically involved on both sides of the body.

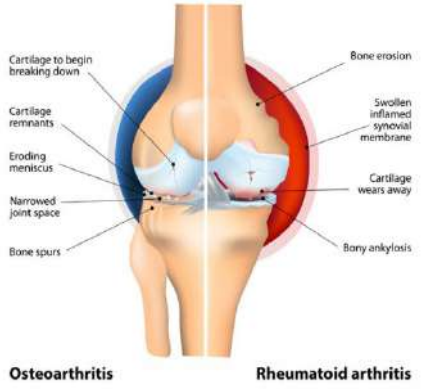

Figure:1 Osteoarthritis and Rheumatoid arthritis

SYMPTOMS AND CAUSES

The most common arthritis symptoms and signs include:

- Joint pain.
- Stiffness or reduced range of motion (how far you can move a joint).
- Swelling (inflammation).
- Skin discoloration.
- Tenderness or sensitivity to touch around a joint.
- A feeling of heat or warmth near your joints

Where you experience symptoms depends on which type of arthritis you have, and which of your joints it affects. Some types of arthritis cause symptoms in waves that come and go called flares or flare-ups. Others make your joints feel painful or stiff all the time, or after being physically activity. The symptoms of a rheumatoid arthritis flare aren't much different from the symptoms of rheumatoid arthritis. But people with RA have ups

and downs. A flare is a time when you have significant symptoms after feeling better for a while. With treatment, you'll likely have periods of time when you feel better. Then, stress, changes in weather, certain foods or infections trigger a period of increased disease activity. Although you can't prevent flares altogether, there are steps you can take to help you manage them. It might help to write your symptoms down every day in a journal, along with what's going on in your life. Share this journal with your rheumatologist, who may help you identify triggers. Then you can work to manage those triggers.

Risk Factors

Anyone can develop arthritis, but some factors may make you more likely to, including:

Tobacco use:

Smoking and using other tobacco products increases your risk.

Family history:

People whose biological family members have arthritis are more likely to develop it.

Activity level:

You might be more likely to have arthritis if you aren't physically active regularly.

Other health conditions:

Having autoimmune diseases, obesity or any condition that affects your joints increases the chances you'll develop arthritis.

Some people have a higher arthritis risk, including:

- People older than 50.
- People assigned female at birth (AFAB).
- Athletes, especially those who play contact sports.

People who have physically demanding jobs or do work that puts a lot of stress on their joints (standing, crouching, being on your hands and knees for a long time etc.) arthritis can develop at any age. When it starts depends on which type you have and what's causing it. In general, osteoarthritis affects adults older than 50. Rheumatoid arthritis usually develops in adults age 30 to 60.

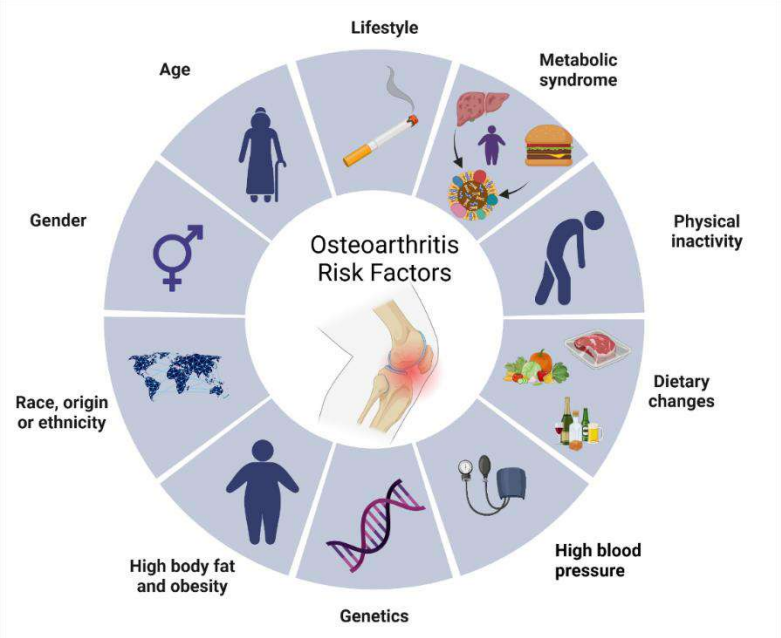

Figure: 2 Risk factor of Osteoarthritis

SUSTAINED RELEASE DRUG DELIVERY SYSTEM

A number of terms have been used to describe the oral dosage forms that represent modified release properties; which include delayed release, repeated action, prolonged release, sustained release, extended release and controlled release. Each drug delivery system is focused at

eliminating the cyclical changes in plasma drug concentration seen after administration of conventional delivery systems. Modified release dosage forms are designed to provide quick achievement of a drug plasma level that remains constant at a value within the therapeutic range of a drug for a significant period of time or achievement of a plasma concentration of a drug that delivers at a slow rate (i.e. sustained release) that stays within the therapeutic range for a longer period of time. Based on the assumption that a drug, which is to be incorporated into a modified release dosage form, confers upon the body characteristics of a one- compartment open model, then the basic kinetic design of such a product may be assumed to contain two portions, one that provides the initial loading dose, and one that provides the maintenance or sustained dose.

DIFFERENT TYPES OF SUSTAINED RELEASE SYSTEMS:

1. Diffusion sustained system.
i. Reservoir type
ii. Matrix type.
2. Dissolution sustained system.
i. Reservoir type.
ii. Matrix type.

SOLUBILITY ANALYSIS

Table : 1 Data for solubility of drug

Sr. No.	Solvents	Solubility
1	Distilled water	Insoluble
2	Ether	Soluble
3	Acetone	Soluble
4	Ethanol	Soluble
5	Castor oil	Soluble

METHODOLOGY : Matrix Method

Extraction of mucilage

The fresh leaves of Hibiscus rosa-sinensis were collected and washed repeatedly with water. The leaves were then crushed and then kept for soaking for 5-6 h. The leaves were boiled for 30 min and left to stand for 1 h for complete release of the mucilage. The mucilage was extracted using a muslin cloth bag to remove the marc from the solution. Acetone (three times the volume of the filtrate) was added to precipitate the mucilage. The mucilage was separated, dried in an oven at35C, collected, grounded, passed through sieve no #80 and stored in a desiccator at 35 C and 45% relative humidity till use.

Preparation of matrix tablets

Sustained release matrix tablets of indomethacin with Hibiscus rosa-sinensis leaves mucilage were prepared using different drug: mucilage ratios viz.,1:0.15, 1:0.3 and 1:0.45. (Table1)Hibiscus rosa-sinensis leaves mucilage was used as matrix forming material whilemicrocrystalline cellulose as a diluent and Magnesium stearate as a lubricant. All ingredients were passed through sieve #100, weighed and blended. The granules were prepared by wet granulation technique and compressed by using 6mm flat faced punches in a rotatory tablet punching machine.

Table : 2 Formulation For Matrix Tablets Of Indomethacin Using Mucilage Of Hibiscus Rosa-Sinensis Leaves.

Formula	Formulations		
	F1(mg)	F2 (mg)	F3(mg)
Indomethacin	100	100	100
Mucilage	15	30	45
Avicel	130	115	100
Magnesium stearate	5	5	5
Total tablet weight	250	250	250

EVALUATION OF TABLET BLEND

Bulk density: Apparent bulk density was determined by placing pre-sieved drug excipient blend in to a graduated cylinder and measuring the volume and weight as it is.The bulk density of a powder is the ratio of the mass of an untapped powder sample and its volume including the contribution of the interparticle void volume. Hence, the bulk density depends on both the density of powder particles and the spatial arrangement of particles in the powder bed. The bulk density is expressed in grams per millilitre (g/mL) although the international unit is kilogram per cubic metre (1 g/mL = 1000 kg/m3) because the measurements are made using cylinders. It may also be expressed in grams per cubic centimetre (g/cm3). The bulking properties of a powder are dependent upon the preparation, treatment and storage of the sample, i.e. how it was handled. The particles can be packed to have a range of bulk densities and, moreover, the slightest disturbance of the powder bed may result in a changed bulk density. Thus, the bulk density of a powder is often very difficult to measure with good reproducibility and, in reporting the results, it is essential to specify how the determination was made.The bulk density of a powder is determined by measuring the volume of a known mass of powder sample, that may have been passed through a sieve into a graduated cylinder, or by measuring the mass of a known volume of powder that has been passed through a volumeter into a cup or a measuring vessel.

$$Bulk\ density = \frac{Mass\ of\ the\ material}{Volume\ of\ the\ material}$$

EVALUATION OF MATRIX TABLET

Weight variation:

Twenty tablets were randomly selected from each batch individually for the average weight and standard deviation of 20 tablets was calculated as per IP specification for weight variation.

Thickness:

The thickness of the tablet was measured by using screw gauge, Twenty tablet from each batch were randomly selected and thickness were measured.

Hardness:

Hardness was measured using Pfizer hardness tester, tablet from each batch and measured in kg/cm2.

Friability:

Ten tablets were weight and placed in the Roche friabilator and apparatus was rotated at 25 rpm for 4 min. After revolution the tablets were dusted and weighedto check that the variation is less than less than 1%.

Drug content uniformity:

This test is performed by taking twenty tablets randomly, weighed and powdered. A quantity of powdered tablet equal to 250 mg of Indomethacin was dissolved in phosphate buffer pH 7.2 in100ml

volumetric flask. The so formed sample was diluted and the absorbance was measured at 265.5 nm using phosphate buffer pH 7.2 as blank and the % drug content was estimated.

Swelling index:

The swelling index of the formulation was carried out by taking one tablet from each batch and placed in a Petridis containing phosphate buffer pH 7.2 At the end of 1h, the tablet was withdrawn, kept on a tissue paper and weighed. The weighing carried out for a period of 5h .

In-Vitro dissolution Study:

The study was carried out in 900 ml of phosphate buffer pH 7.2 at 75 Rpm, which was maintained at 37oC ±0.5oC using the USP apparatus type II (ElectrolabDisso 8000).5 ml samples were withdrawn at regular intervals of 1 hr and the absorbance was measured at 265.5nm using Shimadzu UV spectrophotometer 1700. Sink condition was maintained by replacing with fresh buffer medium. The dissolution study was carried out for 8 hrs followed by mathematical treatment of the solved dissolution data.

RESULT AND DISCUSSION

The extracted mucilage of Hibiscus rosa-sinensis was studied for the desired physical properties and results are shown in Table 3. Matrix tablet each containing 100 mg of Indomethacin were prepared using dried mucilage of Hibiscus rosa-sinensis leaves in various ratio of 1:0.15, 1:0.3, 1:0.45 (drug: mucilage).

Table: 3 Flow properties of dried Hibiscus rosa-sinensis leave mucilage

PARAMETERS	VALUE
Bulk density(g/ml)	0.42
Tapped density(g/ml)	0.44
Carr's index (%)	4.54%
Hausner's ratio	1.047
Angle of repose	23°14'

The pre-compression parameters of granules analysis likebulk density, tapped density, Carr's index, Hausner's ratio and results are shown in Table 4. The bulk density and tapped density ranged from 0.92 to 0.45 g/ml and 1.3 to 1.05 g/ml. Carr's index and Hausner's ratio ranges from0.58 to 0.33 and 2.4 to 1.5 respectively indicating good flowability of granules. Post compression parameters like thickness, hardness, friability and drug content are shown in Table 5. Hardness and friability ranged from 5.8 to 6.8 kg/cm2 and 0.8 to 0.4%. Drug content was ranging from 82% to 96%.

Table: 4 Pre-compression parameters of the granules

Formulation Code	Bulk density(g/ml)	Tapped density(g/ml)	Carr's index (%)	Hausner's ratio	Angle of repose (θ)	
					Without glidant	With glidant
F1	0.92	1.375	0.33	1.5	15θ 26'	14 θ 37'
F2	0.45	1.08	0.58	2.4	17 θ 28'	15 θ 36'
F3	0.515	1.05	0.559	2.03	18 θ 17'	17 θ 25'

Table: 5 Post-compression parameters of tablets

Sr. No	Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
1	F1	3.75	5.8	0.4	82
2	F2	3.70	6.2	0.8	90
3	F3	3.64	5.7	0.4	96

CONCLUSION

The study deals with the investigation of release retardant effect of Hibiscus rosa-sinensis mucilage when formulated as a matrix tablet. The mucilage exhibited an appreciable physicochemical properties and suited best for the development of sustained release tablets as indicated by the drug release studies. This can be used as a potential natural source over the synthetic release retardant. Hence, Hibiscus rosa-sinensis could be employed as a release rate retardant for sustaining the drug release from the formulation. Thus, Matrix tablets of indomethacin formulated by using Hibiscus mucilage as a release retardant could be employed for retardant drug release. One of the most important (NSAID) non-steroidal anti-inflammatory drug-containing the indol core is represented by the indomethacin. This highly relevant compound has been used for the last 50 years with excellent pharmacological results. Arthritis is most prevalent disorder and Indomethacin is choice of drug for arthritis. Oral route is most preferred route of drug administration and tablets are the more convenient dosage form.

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