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Original Research Article

Bilayer Drug Delivery: A Promising Role In Rheumatoid Arthritis

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ABSTRACT: -
Bilayer tablet is an advanced form of tablet design and it's very useful in treatment of chronic diseases and their associated adverse disorders. It's also helpful in treatment where more than one drug is indulged eg. Diabetic, Rheumatoid arthritis. Now a day's many type of marketed bilayer preparation are available which shows a tremendous result to treat chronic disease. Bilayer tablets are used to control different types of successful drug release rate. In this review we discussed on the rheumatoid arthritis, possible treatment, how to bi-layer tablet helpful in RA treatment, bilayer formulation methods, etc. pharmaceutical incompatibility, sustain release, immediate release

Keywords: Bilayer Tablets, chronic disease, NSAIDs, Immediate release, Sustain release, Chronobiological, Arthritis

INTRODUCTION :-

Arthritis (Artho; joint, itis; inflammation) is a chronic disease occurs in every age group and gender. Arthritis is divided mainly a. **Osteoarthritis**, b**. Inflammation arthritis** (rheumatoid arthritis). Arthritis refers to joint disorder that involves inflammation and pain, there are more than 100 types of arthritis occurs during lifespan. RA was discovered by British rheumatologist **Dr. Alfred baring Garrod,** in year 1859 [1]. Rheumatoid Arthritis (RA) is a kind of inflammatory disorder that involves chronic autoimmune and painful disability leading lifelong. It is affected all age group but women are more susceptible than men in aged 35 - 55 due to hormonal imbalance. Morning stiffness, pain, inflammation, loss of energy, lack of appetite, low grade fever (Rheumatoid fever), loss of cartilage, erosion of bones are most common symptoms of RA. Most of affected body parts are articular cartilage destructions, ankylosis (fusion of joints), and inflammation in synovial membrane of hand, feet, and joint of shoulders, knee, cervical spine. It also affects many more organs of body such as skin (rheumatoid nodule), lungs (fibrosis), kidneys (Renal amyloidosis), heart and blood vessels (myocardial infarction) etc[2].

Statistically, approximate 22% 0f U.S. adults aged 18 or older diagnosed arthritis patients. It is estimated that 14% adult (aged 18- 25), 34% (adult aged 34-64) suffering from osteoarthritis and 1.5 million U.S. adults have rheumatoid arthritis. Arthritis killed all age group people during 20 years period of 1979-1998 with 146,377 deaths are recorded with arthritis and other rheumatic conditions. [1] Arthritis creates difficulty in physical activities; it also increases obesity, risk of depression, and psychological fear from pain. Possible management of rheumatoid arthritis changing life style like including exercise, work out, jogging, yoga in daily routine to manage body

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weight and stay healthy, enrich diet with lots of anti-oxidants such as green vegetables, vit A, vit D etc[1].

Treatments used in RA: -RA is a chronic painful disability lead lifelong, management of RA can be done by either by changing lifestyle, or by drugs. There is no cure of Rheumatoid Arthritis but pain and inflammation can manage as follows

Management of lifestyle: -Proper management of lifestyle includes Regular exercises such as walking, swimming, yoga, riding; healthy diet can be minimized the risk of RA. Occupational therapies like physiotherapy also a part of management of RA.

Surgery: - Removal of the joint lining (snovectomy) or total joint replacement (Arthoplastices) surgeries serves in Surgery is a last option when no drug is useful in treatment of RA.

Treatment by drugs:- There are several of drug treatment is used in RA. At initial State reduced pain and inflammation in joint can be used Non steroidal anti inflammatory drugs (NSAIDs). Next stage of RA, disease modifying anti-rheumatic drugs (DMARDs) such as methotrexate, sulfasalazine etc and Biological agents can be used.

General properties of bi-layer tablet dosage forms

1. It should have graceful product identity free of defects like chips, cracks, discoloration and contamination.
2. Should have sufficient strength to with stand mechanical shock during its production, packaging, shipping and dispensing.
3. Should have physical and chemical stability.
4. The bi-layer tablet must release drug in a expectable and reproducible manner.
5. Must have a chemical stability shelf life, so as not to follow alteration of the medicinal agents.

Bilayered tablets: Quality and GMP requirements

To produce a quality bi-layered tablet, in a validated and GMP way, it is important to select a Bilayered tablet press is capable of:

- Preventing capping and separation of the two individual layers that constitute the bi-layer tablet.
- Providing sufficient tablet hardness.
- Preventing cross contamination between the two layers.
- High yield Accurate and individual weight control of the two layers.
- Precise and individual weight control of the two layers.

Methods:-

Type	Characteristics
Tab-in-a-Cap	Multiple release profiles are easily achieved by filling immediate release formulation (prostaglandin analogue) in outer larger capsule and sustained or controlled release formulation (NSAID) in inner smaller tablet.
ACCUBREAK	ACCU-BREAK tablet technology use aninactive layer (segment) as the break region. The layer containing drug can be scored into 2, 3 or 4 equal segments, all adjacent to aninactive breakable support segment. Thus, a tablet could be broken easily into the specific dose desired.
Spheroids/	Controlled-release beads/granules in the range from 1 to 2

Pallets/ Bead	mm containing drugs may be formulated. Each bead begins as an inert core onto which the drug is applied. Drug release from these beads occurs by a diffusion process in a controlled, predetermined manner. These dosage form enable high drug loading and granules produces beads that are of controlled size and density with a defined-based granulation extrusion and spheronisation techniques.
Delayed release (Lag) based technology	It is used to release the drug from the tablet after a pre-determined lag-time that isindependent of food or pH.It can additionally be used for multiple pulse delivery of one or more drugs with predetermined time intervals between the pulses.
OROS (Osmotic and Chronset)	OROS delivery systems consist of the pushpull system is comprised of a bilayer or trilayer tablet core consisting of one push layer and one or more drugs layers. The drug layer and the osmotic engine are encased in hard capsule which is surrounded by the rate controlling semi permeable membrane. A barrier layer composed of an inert substance separates the drug layer from osmotic engine. Using this technology, the drug formulation is completely protected from chemical and enzymatic degradation in the GIT before release, and the timing of release isunaffected by GIT contents.
One Step Dry Coating Technology (OSDrC)	OSDrC technology allows placement of any number of cores of any shape into the tablet just where they need to be positioned for optimum delivery of APIs. This technology opens the door to new world of pharmaceutical tablet manufacturing with advantages like uniqueness, high quality, low cost and innovativeness.
Diffucaps/ Diffutabs	In this technology, a unit dosage form, such as a capsule for delivering drugs into the body in a circadian release fashion, is comprised of one or more populations of drug-containing particles (beads, pellets, Granules, etc.). Drug profiles are created by layering an active drug onto a neutral core such as cellulose spheres and then one or more rate-controlling, functional membranes are applied.

CONCLUSION: -

Combination Drug Delivery plays a vital role to minimize side effects or provide various pharmacokinetic Profiles in single tablet include Patient Compliance, Increases Bioavalibity, and Reduce Dose Frequency. Bilayer tablet technology is used to overcome the limitations of single layered tablets and this technique is cost effective, safe and reproducible. In treatment of chronic disease like rheumatoid arthritis, diabetics etc bilayer system is a convenient way for manufacturing purpose and for ease of patient's drug administration. . Rheumatoid Arthritis (RA) is a chronic autoimmune painful inflammatory disease generally occurs in synovial membrane and surrounding tissues. It is long term painful disability which leads to the destruction of auricular cartilage. It also affect multiple organ of body such as lungs, heart, kidney, eye, blood vessels etc. NSAIDs are commonly used medication in the treatment of pain and inflammation in joints. Chronobiological behavior of disease plays a prominent role in morning pain and stiffness. Time related manifestation

of related symptoms leads to an emergence of Chronotherapis often used in the treatment of morning pain. Now a day various pharmaceutical scientists rationally trying to develop Bilayer Drug Delivery as combination therapy in the treatment of long term disability and disorders. Promising feature of this Bilayer Drug Delivery system shall have varied pharmacokinetic drug release pattern in single unit as "immediate" and "sustain" release. It can be loaded with more than one active molecules and formulated to achieve desired drug release profile.

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