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Review article

Review on treatment of arthritis and gout via topical route of skin

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ABSTRACT

In arthritis suffering patients there is no choice except pain killer because of continuous pain if continuous use of pain killer they affected all organ, damage kidney and most hazardous action of NSAID class drug is produce ulcer so for avoiding continuous oral medication. It is necessary to formulate a new kind of formulation which not taken orally and produce a specific and effective action without producing side effects. So, transdermal route and Transdermal Patch is one of the best solutions for this problem. Transdermal drug delivery is a painless, convenient, and potentially effective way to deliver regular doses of many medications. Dermal patches are the most common form of transdermal delivery of drugs. Ten years ago, the nicotine patch had revolutionized smoking cessation; patients were being treated with nitroglycerin for angina, clonidine for hypertension, scopolamine for motion sickness. This article provides valuable information regarding the Transdermal drug delivery system and about arthritis and NSAIDs.

Keywords: penetration, lipophilicity, gout, joint pain, treat.

INTRODUCTION

SKIN

The skin is the largest organ of the body, Human skin consists of three main layers: the epidermis, dermis, and hypodermis. The epidermis, in particular the stratum corneum, acts as the major barrier to drug absorption. The thickness of the epidermis varies from 0.06 mm on eyelids to 0.8 mm on the soles of the feet. It exerts multiple vital protective functions against environmental aggressions.

Drug absorption into the systemic circulation is rapid due to the large capillary bed. Epidermis is divided into 7 layers. Stratum corneum is the thickest layer. The dermis is the thickest layer of the skin (3–5 mm) and possesses hair follicles, sweat glands, nerve endings, and blood and lymph vessels. It acts as the systemic absorption site for drugs [1].

Skin as a Barrier

The stratum corneum is a horny layer of the skin; the thickness of this layer is between 10 -15 µm and consists of 10-25 layers and consist of mainly proteins. There can be found intercellular lamellar lipids between these thin layers. They are residue of the membrane surrounding each epidermal cell and they come into existence when the epidermal cells are embodied. This lipid contains ceramides, free sterols, free acids, sterol esters, triglycerides, etc. These lipids are able to organize themselves into membrane bilayers, although they do not contain any Phospholipids. All the components of the interstitial lipids contribute to the barrier function of the stratum corneum [2].

Different layers of skin

The transdermal delivery of the drugs has three major pathways in the stratum corneum.

Para cellular

Tran cellular

Appendage

The paracellular pathway involves the lamellar lipids into the transport of drugs, which are essentially responsible for the sticking of the epidermal cells. During the transcellular transportation the drugs pass through the cells of the stratum corneum. Drugs which diffuse through the sebaceous glands come first into the dermis and then into the hypodermis [3].

Transdermal Therapeutic Systems

The drug content of transdermal therapeutic systems (TTS) is able to penetrate through the different layers of the skin to reach the systemic circulation and the organ, where the drug is ready to give its therapeutic effect. There are many advantages of these systems.

There can be also drugs applied, which could be used only via I.V Injection or infusion because of the metabolization

They lower the risk of microbiological contamination

The effect of food and drinks does not affect the liberation of the drug

Drugs with short biological half time can be also applied

Enhance the patient compliance.

The eventually negative effect of the drug can be terminated with the removal of the Patches.

The drug avoids the liver, which results in delayed metabolization of the drug

It does not oppress the liver and the GI tract

It enhances the biological half time of the drug (through avoiding the liver)

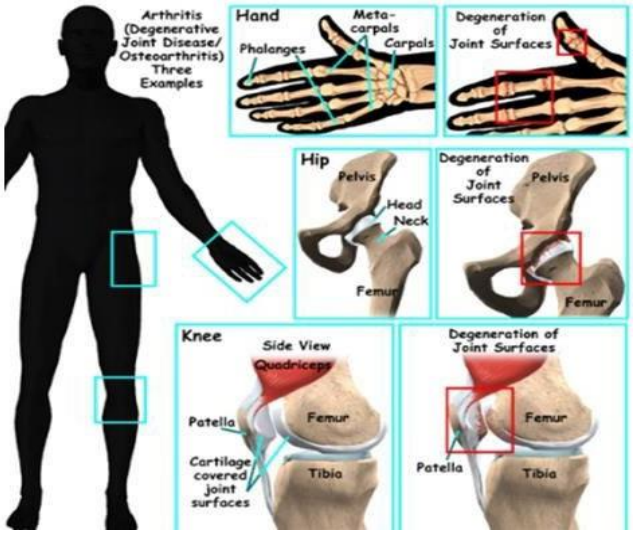
It results in higher bioavailability of the drug [4].

Arthritis

Arthritis literally means joint inflammation. "Arth" refers to the joints, and "itis" refers to inflammation. Arthritis is not a single disease. There are more than

100 different types of arthritis affecting people of all ages, including about 300,000 children.

The most common form, osteoarthritis is a result of trauma to the joint, infection of the joint, or age. Other forms of arthritis are rheumatoid arthritis, psoriatic arthritis. Pain is often a constant and may be localized to the joint affected. The pain from arthritis is due to inflammation that occurs around the joint, damage to the joint from disease, daily wear and tear of joint, muscle strains caused by forceful movements against stiff painful joints and fatigue [5].



Classification

Primary forms of arthritis

Osteoarthritis

Rheumatoid arthritis

Gout and pseudo-gout

Septic arthritis

Ankylosing spondylitis

Juvenile idiopathic arthritis

Still's disease

Secondary Forms of Arthritis

Psoriasis (Psoriatic arthritis)

Reactive arthritis

Ehlers-Danlos Syndrome

Haemochromatosis

Hepatitis

Lyme disease

Inflammatory bowel disease (Including Crohn's Disease and Ulcerative Colitis)

Henoch-Schönleinpurpura

Hyperimmunoglobulinemia D with recurrent fever

Sarcoidosis

TNF receptor associated periodic syndrome

Wegener's granulomatosis (and many other vasculitis syndromes)

Familial Mediterranean fever

Systemic lupus erythematosus

Different types of arthritis

Osteoarthritis:-Also called degenerative joint disease, this is the most common type of arthritis, which occurs most often in older people. In extreme cases, the cartilage can completely wear away, leaving nothing to protect the bones in a joint, causing bone-on-bone contact. Bones may also bulge, or stick out at the end of a joint, called a bone spur.

Rheumatoid Arthritis:-This is an autoimmune disease in which the body's immune system attacks healthy joints, tissues, and organs. Occurring most often in women of childbearing age, this disease inflames the lining of joints. It can cause pain, stiffness, swelling, and loss of function in joints. When severe, rheumatoid arthritis can deform, or change, a joint [6, 7].

The warning signs for arthritis include

Pain, Swelling, Stiffness, Difficulty moving one or more joints, Joint Popping/Cracking and Arthritis, Limited Joint Motion, Bone Spurs.

Most common form of arthritis

The most common form of arthritis is osteoarthritis, sometimes referred to as wear-and-tear arthritis or degenerative joint disease. The primary form of osteoarthritis is usually related to aging, but osteoarthritis can also result from injury or obesity.

Causes of arthritis

Arthritis is caused by a variety of factor including;

Joints stability

Injuries

Age-related

Toxins

Microbes

Altered biochemistry

Hormonal factors And genetics

Dietary

Even dental factors have also been found to bring on the condition.

In recent years, research conducted by rheumatologists and concluded that some patients can experiences allergy-induced arthritis.

Stress can also be a major factor because it disturbs the body hormonal balance. Stress related changes in the chemical levels of cortisol can often lead to changes in the immune system. This sequence often occurs in women undergoing in menopause. Lyme diseases can also causes arthritis symptoms, especially infectious arthritis. Presumably caused by bacteria. Additionally, maintaining overall good health and strength with exercise and good nutrition can be helpful in preventing joint disease.

Get to and stay at a healthy weight.

Get regular exercise. Don't overdo it, though. If feel pain, stop [8].

Prevent falls and sports injuries

Treatment depends on the type and how severe it is. In general, treatment includes:

An exercise program for your needs. Exercises done in water are very helpful and soothing.

Medicines to help relieve pain and reduce swelling.

Healthy diet. Weight loss, if overweight.

Physical therapy.

Leech therapy.

Knee taping.

Surgery. When needed, damaged joints can be repaired or replaced with artificial ones.

Self-Care / Prevention

Follow your doctor's advice on exercise.

Take OTC and prescribed medicines as doctor advises, about supplements, such as glucosamine and flaxseed oil. Discuss products that promise to cure arthritis with your doctor. Do these before you try any of them.

Follow a healthy diet. Lose weight if you are overweight. Do not fast, though. This can raise uric acid levels and increase the risk for gout.

Don't do activities that put too much stress on joints. Take regular breaks. Protect the joints from injury. Wear knee pads, etc.

NSAID

Since the synthesis of aspirin in 1897, aspirin-like or Non-steroidal antiinflammatory drugs (NSAIDs) have been the mainstay of therapy for rheumatoid arthritis. Although of diverse chemical structure, these drugs not only exhibit the same antipyretic, analgesic and antiinflammatory therapeutic actions, but they also manifest identical toxic actions on the gastric mucosa and the kidney.(19) Recent debate has highlighted severe cardiovascular side effects from COX-2 selective Nonsteroidal anti-inflammatory drugs (COX-2 inhibitors or coxibs). This has led to a withdrawal from the New Zealand (NZ) market of rofecoxib and Valdecoxib in accordance with international recommendations. NSAID also are a common treatment for chronic (long-term) health problems such as arthritis (rheumatoid arthritis, osteoarthritis and others). Examples of drugs used to treat arthritis [9].

CLASSIFICATION OF NSAIDs

COX-1 SELECTIVE INHIBITORS

Acetylsalicylic acid at low dosage

NONSELECTIVE COX INHIBITORS

Acetylsalicylic acid at high dosage

Diclofenac

Aceclofenac

Ibuprofen

Ketoprofen

Flurbiprofen

Indomethacin

Piroxicam

Naproxen

MORE COX-2 SELECTIVE INHIBITORS

Nimesulide

Etodolak

Meloxicam

Nabumeton

COX-2 SELECTIVE INHIBITORS

Celecoxib

Etorcoxib

Valdecoxib

Rofecoxib

Firocoxib

FENAMIC ACID DERIVATIVES (FENAMATES) (non selectivescox inhibitors)

Mefenamic acid

Meclofenamic acid

Flufenamic acid

Anti-inflammatory effects of NSAID

The use of this Nonsteroidal anti-inflammatory medication has been shown in scientific studies to accelerate the particular cartilage breakdown in osteoarthritis. This effect of NSAID is due to the inhibitionof theenzyme COX, which converts arachidonic acid to prostaglandins, TXA2 and prostacyclin.

Acetylsalicylicacid irreversibly inactivates COX-1 and COX-2 by acetylation of a specific serine resident. Other NSAID reversibly inhibit COX- and COX-2 .Additional anti- inflammatory mechanism may include:

Interference with the potentiative action of other mediators of inflammation – bradykinin, histamine, serotonin

Modulation of T-cell function

Stabilization of lysosomal membranes

Inhibition of chemotaxis [10].

Analgesic effect of nsaid

Though NSAIDs are chemically disparate, they produce their therapeutic effects by inhibit COX enzymes COX1 and COX2. COX1 is considered important in tissue homeostasis. COX2 is transcriptionally induced by cytokines and is important in the development of inflammation. NSAIDs have been developed to target these cycloxygenase, including acetylsalicylate (aspirin), ibuprofen, etc. NSAID prevent the potentiating action of prostaglandins on endogenous mediators of peripheral nerve stimulation.

Clinical uses of nsaid

1Analgesia

2Inflammation

Antipyresis

Antiplateled Effect

Cancer preventive agents

NSAID are classified as mild analgesics. Although this designation says something about the potency of NSAID, it is misleading without the qualification that a major reason for the analgesic effect of NSAID is that they inhibit inflammation. Examples of the former include a variety of rheumatologic conditions, such as ankylosing spondylitis and rheumatoid arthritis. NSAID are widely used in the treatment of acute musculoskeletal injuries, and there is evidence for their ability to provide symptomatic relief of conditions such as acute low back pain. NSAID are also commonly used in chronic musculoskeletal pain.

Adverse effects of nsaid

Serious cardiovascular side effects and complications.

Gastrointestinal effects: Abdominal pain, gastric and duodenal ulcer, diarrhea, pancreatis gastrointestinal hemorrhage.

Hepatotoxicity.

Upper GI tract injury is a major side effect of NSAID and dyspepsia. Gastroduodenal ulcers [11].

Pharmacodynamic interaction nsaid with other drugs

The pharmacodynamic interaction between quinolones and other GABA inhibitors is extremely poorly.

NSAID with hypotensive drugs (β- blockers, ACE-inhhibitors, diuretics) = ↓ hypotensive effect

NSAID with ethanol = ↑risk of bleeding

from gastrointestinal tract

NSAID with ticlopidine or clopidogrel =

↑risk of bleeding

NSAID with lithium = ↑lithium toxicity NSAID with cyclosporine or ACE- inhibitors or takrolimus= ↑nephrotoxicity of drugs

NSAID withfluoroquinolons = ↑ toxic action of fluoroquinolons on CNS

NSAID with oralantidiabeticdrugs =↑ risk of hypoglycemia

NSAID with cumarines = ↑risk of bleeding from gastrointestinal tract [11].

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