Arthritis and Transdermal Glucosamine (Rahamin®): A brief introduction

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Abstract

There are more than 100 types of arthritis and its related conditions. The goal of arthritis treatment is to reduce joint pain and inflammation. In this regard, glucosamine is known to stop degenerative process of osteoarthritis. Topically applied products, compared with those taken orally, are safer and cause less complications. Various researches on different kinds of glucosamine showed that skin permeation of the topical dosage form improves pain scale more effectively in comparison with placebo after 6 weeks. The results have shown that transdermal glucosamine is more cost-effective than oral dosage form. Rahamin® is an Iranian brand of transdermal glucosamine which contains Glucosamine, Devil's claw dry extract, MSM and vegetable oils.

Keywords: Transdermal, Glucosamine, Rahamin, Arthritis
Introduction

Pains resulting from degenerative musculoskeletal diseases and disorders are rising due to increasing number of aging population, obesity and occupational stress, and might impose considerable financial burden on individual and social economy. Dealing with pain is one of the hard parts of treating these kinds of diseases. There are more than 100 types of arthritis and its related conditions such as osteoarthritis (OA) (degenerative arthritis), rheumatoid arthritis (RA) and juvenile inflammatory arthritis (JIA), as well as gout, psoriatic arthritis, fibromyalgia, repetitive strain injury (RSI), muscular stress and back pain (1,2). The goal of arthritis treatment is to reduce joint pain and inflammation, while improving and maintaining its function and preventing from its damage. The Most frequently applied treatments are analgesics such as oral non-steroidal anti-inflammatory drugs (NSAIDS), corticosteroids, centrally acting medicines, supplements, physiotherapy and surgery as the last option (3). In recent years, glucosamine has also been introduced as a safe over-the-counter supplement for OA and related ailments with an estimated annual sale of exceeding 700 million dollars only in the United States (4).

Transdermal Glucosamine and Patients’ Compliance

After many years of research, Dr Jonathan Obaje, who is originally from Singapore, invented a transdermal glucosamine cream in 2003 based on his US patented technology (5). Glucosamine is known to stop the degenerative process of OA. As most of its formulations on the market are in oral form, an alternative formulation such as a transdermal delivery system (TDS) could increase patients’ compliance. Considering that glucosamine is naturally acidic, taking oral glucosamine tablets and capsules over extended periods of time might cause gastric irritation and ulcer. In addition, oral glucosamine has a very low bioavailability (little absorption by blood). Hence, its effective intra-articular concentration may not be achieved by taking about 1500 mg daily of oral glucosamine after several months (6-9). Topically applied products, compared with those taken orally,
are safer and cause less complications. Joint treatment medications will not work effectively unless they are absorbed well.

**Skin Permeation of Glucosamine**

Evaluation of the stability of Glucosamine Sulphate at different pH values showed the compound to be most stable at a pH of 5.0. The degradation rate constant at 25°C was estimated to be $5.93 \times 10^{-6}$ hr$^{-1}$ ($t_{90} \approx 2.03$ years) in a pH 5 buffer solution. Due to its hydrophilic characteristic, low skin permeability was expected. However, the skin permeation rate was determined to be 13.27 µg/cm$^2$/hr at 5% concentration (10). In another study Glucosamine hydrochloride (GL-HCl) formulations such as o/w cream, liposome suspension, liposomal gel, and liquid crystalline vehicles were prepared and compared with evaluate transdermal flux of GL-HCl. The liquid crystalline vehicles were more effective in increasing the skin permeation of GL-HCl than o/w cream and liposomal vehicles. The skin permeation of GL-HCl was further increased by employing both oleic acid and polyethylene glycol 200 (11). Another study showed that GL-HCl permeates through human skin with a flux of $1.497 \pm 0.42$ µg/cm$^2$/h, a permeability coefficient of $5.66 \pm 1.6 \times 10^{-6}$ cm h$^{-1}$ and with a lag time of $10.9 \pm 4.6$ h (12).

Transdermal permeation of N-acetyl-D-glucosamine (NAG), a metabolite of glucosamine was also examined. Permeability of NAG in various enhancer suspensions was evaluated by using shed snake skin as a model membrane via Franz-type cell diffusion studies. Negligible permeability was observed for NAG in neat solutions of known membrane permeation enhancers such as ethanol, oleic acid, isopropyl myristate, and isopropyl palmitate, as well as from saturated solutions of NAG in water or phosphate buffer. Permeability measurements obtained from saturated solutions of NAG in DMSO and in phosphate buffer/ethanol solutions containing 2%, 5%, 10%, 25%, and 50% ethanol demonstrated an excellent permeation. Permeability coefficients of the phosphate buffer/ethanol solutions at 5%, 10%, and 25% were about threefold larger in value as those for saturated DMSO solution, whereas the 2% and 50% solution values were lower (13). Results of a randomized double blind study on the effects of a topical cream containing Glucosamine Sulfate on osteoarthritis of the
knee in Western Ontario and McMaster Universities revealed a greater mean pain reduction in glucosamine/chondroitin preparation group (mean change - 3.4 cm, SD 2.6 cm) compared with the placebo group (mean change - 1.6 cm, SD 2.7 cm) after 8 weeks. The difference between mean reduction from baseline of active and placebo groups was 1.2 (95 per cent CI 0.1 to 2.4, p = 0.03) after 4 weeks and 1.8 (95 percent CI for difference between groups, 0.6 to 2.9 cm; p = 0.002) after 8 weeks.

Topical application of glucosamine and chondroitin sulfate is effective in knee OA pain relief and results in obvious improvement within 4 weeks. Long term use of glucosamine may reduce radiographic signs of knee OA progression, suggesting that it may be a chondro-protective, disease modifying agent (14). Clinical assessment of glucosamine named Urah® cream after 6 weeks showed a remarkable improvement of 72% in pain scale. 1g of Urah cream had a bioequivalence of about 2,000 mg, equivalent to 4 tablets swallowed orally. Urah cream therapy showed to be a cheaper alternative to oral therapy. In addition to being cost-effective, it did not have any side effects such as gastric irritations associated with oral glucosamine tablets and capsules (15).

**Brands of Transdermal Glucosamine in the Market**

URAH cream®, Sporting cream®, Optimal joint health cream®, Gluco Balm cream®, MONTI-RELIEF®

**Rahamin®**

Rahamin® is a transdermal glucosamine manufactured by Raha Pharmaceutical Company. It contains glucosamine sulfate, methyl sulfonyl methan (MSM), Devil's claw dry extract, olive oil, grape seed oil, peppermint oil, evening primrose oil, boswelia resin, menthol and camphor.

Devil's claw dry extract is found to exert significant dose-dependent anti-inflammatory and analgesic effects on the carrageen-induced oedema and writhing tests respectively. Devil's
claw is approved as a nonprescription medicine by the German Commission E and is used to treat arthritis, and relieve lower back, knee and hip pain. It is also used to treat a number of ailments including osteoarthritis, rheumatoid arthritis, gout, bursitis, tendonitis, loss of appetite and digestive disorders.

Boswellic acids inhibit the leukoterian synthesis via 5-lipoxygenase to act as anti-inflammatory agent. Evening primrose oil contains linoleic acid, gamma linolenic acid, and vitamin E. Gamma Linolenic acid is a precursor of prostaglandin E and several other active substances and is demonstrated to be the constituent of the oil responsible for its therapeutic effects. Phenolics found in olive oil possess lipoxygenase inhibitory, prostaglandine sparing and anti-oxidant properties. Grape seed oil contains proanocyanidin which has anti-inflammatory effect. It has free radical scavenging and anti lipid peroxidation effects and inhibits the formation of inflammatory cytokines (16).

Besides, the oils and MSM of this product increase absorption of glucosamine. MSM is methyl sulfonyl methane, which is a very close cousin to DMSO. In fact, DMSO is the raw material from which MSM is manufactured through a very simple process. DMSO has been known as a "penetrant" and a "carrier" since long ago. MSM has the same properties that DMSO has, but not quite so intensely. The liquid mixture of water and MSM will, itself, penetrate through the skin, and will also carry other ingredients with it. It also has anti-inflammatory effect on RA.

Who needs Rahamin® ointment?

- The aged who are suffering from arthritis pains.
- The young who need strong and healthy joints or have experienced joint injuries.
- The Ladies with after-delivery back and neck pains or menopausal pains.
- The professionals with office and job stress pains.
- Rahamin® is a Pain Solution for Every One.
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