## INTRODUCTION

Osteoarthritis (OA), previously called degenerative joint disease, is a complex response of joint tissue to cartilage degradation [1]. OA affects almost all joints, especially weight-bearing and frequently used joints. In primary (idiopathic) OA, no underlying cause is apparent. In secondary OA, various predisposing factors such as trauma, congenital abnormality, or metabolic disorders are present. Although the causes of OA are not known, biomechanical stresses affecting the articular cartilage and subchondral bone and biochemical changes in the articular cartilage and synovial membrane are important in its pathogenesis. Articular cartilage in OA has shown to lose its mechanical resistance, elasticity and smoothness, and is consequently worn out by the movements of the joint, leading to reactive bone remodeling, forming osteophytes, microfractures, subchondral eburnation and pseudocysts and exposure of the articular end of the bone [2]. The consequent roughness of the articular cartilage surfaces elicits secondary inflammatory reactions of the synovial membrane and of the bone. Unlike rheumatoid arthritis and other inflammatory joint diseases, the inflammatory component of OA is relatively mild [3,4]. Clinical manifestations of OA of knee are joint pain, stiffness in the morning or after rest, pain at night, limited joint motion and/or joint deformity. Joint pain in OA may originate not only from synovitis but also from stretching of the joint capsule or ligaments, periosteal irritation due to osteophyte formation, trabecular microfractrures, intraosseous hypertension, or muscle spasm [5-8].

Although there are many treatment modalities for OA of knee including nonpharmacologic therapy (e.g., patient education, weight control, physical and occupational therapy, aerobic exercise programs) and pharmacologic therapy (e.g., intraarticular steroid injections, paracetamol, topical analgesics, NSAIDs and opioid analgesics) [4]. NSAIDs, prostaglandin synthesis inhibitors, are widely prescribed to reduce joint pain and stiffness in OA [9]. Nonetheless, since the inflammatory component of OA is usually minimal, the need for anti-inflammatory effect of NSAIDs in this condition is controversial [10,11]. Although short term trials have demonstrated that NSAIDs are superior to placebo in pain relief in OA of knee [12,13], the efficacy of paracetamol (4 g/day) is proved to be similar to that of ibuprofen, whether ibuprofen is

administered in analgesic (1200 mg/day) or anti-inflammatory doses (2400 mg/day) [14]. In other studies, ibuprofen in a dose of only 1200 mg/day is equivalent to diflunisal, phenylbutazone, indomethacin and meclofenamate in relieving joint pain due to OA [15-18] even when the comparative NSAIDs are given in anti-inflammatory doses [16,18]. Flubiprofen shows no difference in symptomatic treatment of OA of knee when compared to an analgesic nefopam [19], whereas diclofenac is superior to propoxyphene-paracetamol combination in relieving joint pain due to knee OA [20]. Thus, the anti-inflammatory effect of NSAIDs may generally not play an important role in symptomatic treatment of OA of knee. Although NSAIDs are effective in reducing the symptoms of OA, inhibition of prostaglandin biosynthesis is directly related to many common and occasionally severe side effects including gastrointestinal bleeding, hypertension, congestive heart failure, hyperkalemia, and renal insufficiency [21-23]. These disadvantages call for an evaluation of the risks and benefits of the therapy in comparison with less toxic therapy for OA.

Acupuncture, an important branch of alternative medicine, is also an effective treatment for combating pain [24-26]. It is performed by inserting fine needles into particular points on the body and stimulating them by hand maneuver to produce a phenomenon called "needle sensation". In recent years, electroacupuncture (EA), utilizing electric current to stimulate acupuncture points via inserted needles, has been developed. The stimulation parameter adopted is of low frequency and low intensity (in volts or milliamperes) to elicit slight, localized muscle twitches. EA is now widely used, especially in scientific studies, since it is easier to control [24]. Acupuncture is safe and free from serious adverse effects [27]. Adverse effects of acupuncture are local in nature, e.g., contrusion, hematoma, skin and soft tissue infections, etc. The most common adverse effects usually due to unskillful manipulations or unsterilized technique. Nevertheless, the systemic adverse effects of acupuncture are relatively mild when compared to those from the systemic administration of analgesics, especially NSAIDs and opioids [28]. From these reasons, acupuncture is growing in popularity in most Western countries and continues to be a major form of treatment in China and Japan. In the U.S.A., an estimated ten million consultations for acupuncture take place each year [29].

Since the NSAIDs' efficacy in symptomatic treatment of OA of knee depends on the analgesic effect rather than anti-inflammatory effect, paracetamol (pure analgesic drug) has been recently recommended to be the oral first-line drug in management of OA of knee [4]. However, long term use of paracetamol can lead to chronic renal impairment [30]. Thus, the less toxic pain managing procedures (e.g., EA) may be considered to be the alternative treatment of this disease. Even though EA is safe, inexpensive, and effective in combating pain, the role of EA itself in OA of knee is still controversial. Moreover, the comparative studies between EA and analgesics in OA of knee are rare [28]. Thus, the aims of this study were to compare the efficacy and the effects on cartilage markers of EA, diclofenac and their combination in short-term, symptomatic treatment of OA of knee. Diclofenac was used in comparison because it's analgesic effect and efficacy have been shown to be superior [20,31-33] or equal to [34-39] those of pure analgesic drug or other NSAIDs. Moreover, it has been shown that diclofenac exerts its analgesic effect through some mechanisms identical to those of the EA [40-42].