

## SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL EVALUATION OF NEW SCHIFF BASE DERIVATIVES OF KETOPROFEN

Marwan Imad Jihad

Department of Pharmaceutical Chemistry, Baghdad College of Medical Sciences, Iraq.

e-mail : marwan\_alnoori@yahoo.com

(Received 27 November 2019, Revised 21 January 2020, Accepted 30 January 2020)

**ABSTRACT :** In last decades the resistance of many bacterial infections against several antibiotics increased this is attributed to many reasons like misuse of antibiotics in which these medicines prescribed without sensitivity test or can be used without prescription especially in developing countries, in addition to these two main reasons resistance actually acquired in many cases from proper use of antibiotics. So, various attempts were done to synthesize new compounds to overcome this growing problem.

In this work, four Schiff base compounds were synthesized and checked for their antibacterial activity against *Pseudomonas Aeruginosa*, *Escherichia coli*, *Bacillus* and *Staphylococcus aureus*. Schiff base derivatives was selected due to their biological importance and several antibacterial agents were synthesized and examined are imines plus several non-steroidal anti-inflammatory drugs derivatives have antimicrobial activity, for that imine derivatives of ketoprofen synthesized and antibacterial assessment done to them. These derivatives synthesized by reacting four ethyl ester derivatives of amino acids with ketoprofen to give the amide intermediates which then converted to hydrazide derivatives by treating them with hydrazine hydrate, finally these derivatives treated with p-chlorobenzaldehyde to yield the imine or Schiff base compounds that checked for their antibacterial activity. The results show that tested compounds in comparison to standard compound (Ciprofloxacin), exert lower effect against *Escherichia coli* and *Staphylococcus aureus* and nearly comparable effect against *Pseudomonas aeruginosa* and *Bacillus*.

**Key words :** Ketoprofen derivatives, antibacterial activity, Schiff base, imine derivatives.

### INTRODUCTION

In recent years many attention has been directed toward the discovery and development of new antibacterial drugs, especially for infections caused by *Pseudomonas aeruginosa*, *Escherichia coli*, *Bacillus* and *Staphylococcus aureus*, these infections are often spread worldwide despite the use of broad-spectrum antibiotics. The latter abuse and the inappropriate use of anti-infectious agents have led to microbial multi-drug resistance. Faced with this problem, it is imperative to develop new approaches to circumvent this phenomenon, thus the need to discover new classes of drugs with original structures and mechanisms of action (Ragavan *et al*, 2010; Desai *et al*, 2016). Ketoprofen and Ciprofloxacin as reference, DMSO as control and the synthesized compounds (IVa-d) were screened for their antibacterial activity studies against these four pathogens that mentioned above at concentrations of (62.5, 125, 250 and 500 µg/mL) except the control, which used pure. Ketoprofen, 2 (3 benzoylphenyl) propionic acid is a non steroidal anti inflammatory drug (NSAID) with

pronounced analgesic and antipyretic properties via inhibition of the COX enzymes (cox-1 and cox-2 isoforms) which catalyzes the first step of the biosynthesis of prostaglandins (Sieper *et al*, 2008). The first isoform COX-1 is constitutively expressed particularly in the gastrointestinal tract and the kidneys. It is responsible for the physiological production of prostaglandins. The other isoform COX-2 is induced during inflammation process (Elliott *et al*, 2006). Numerous derivatives of ketoprofen and other NSAIDs have been synthesized in order to minimize side effects, prolong plasma half life and increase water solubility or lipophilicity (Bonina *et al*, 2003; Bonina *et al*, 2002). Many studies showed some NSAIDs have good antibacterial action especially ibuprofen and aspirin (Hersh *et al*, 1991; Wang *et al*, 2003). About 9.4 million foodborne illnesses caused by a known pathogen occur annually in the United States and about 1.3 million (14%) of them are caused by *Bacillus cereus* or *Staphylococcus aureus* (Scallan *et al*, 2011). The human pathogen *Staphylococcus aureus* is a major cause of community- and hospital-acquired skin, respiratory,