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Synthesis and evaluation of some newer hybrids of diclofenac acid and 1, 3, 4-oxadiazole: Reduction of ulceration with anti-inflammatory activity

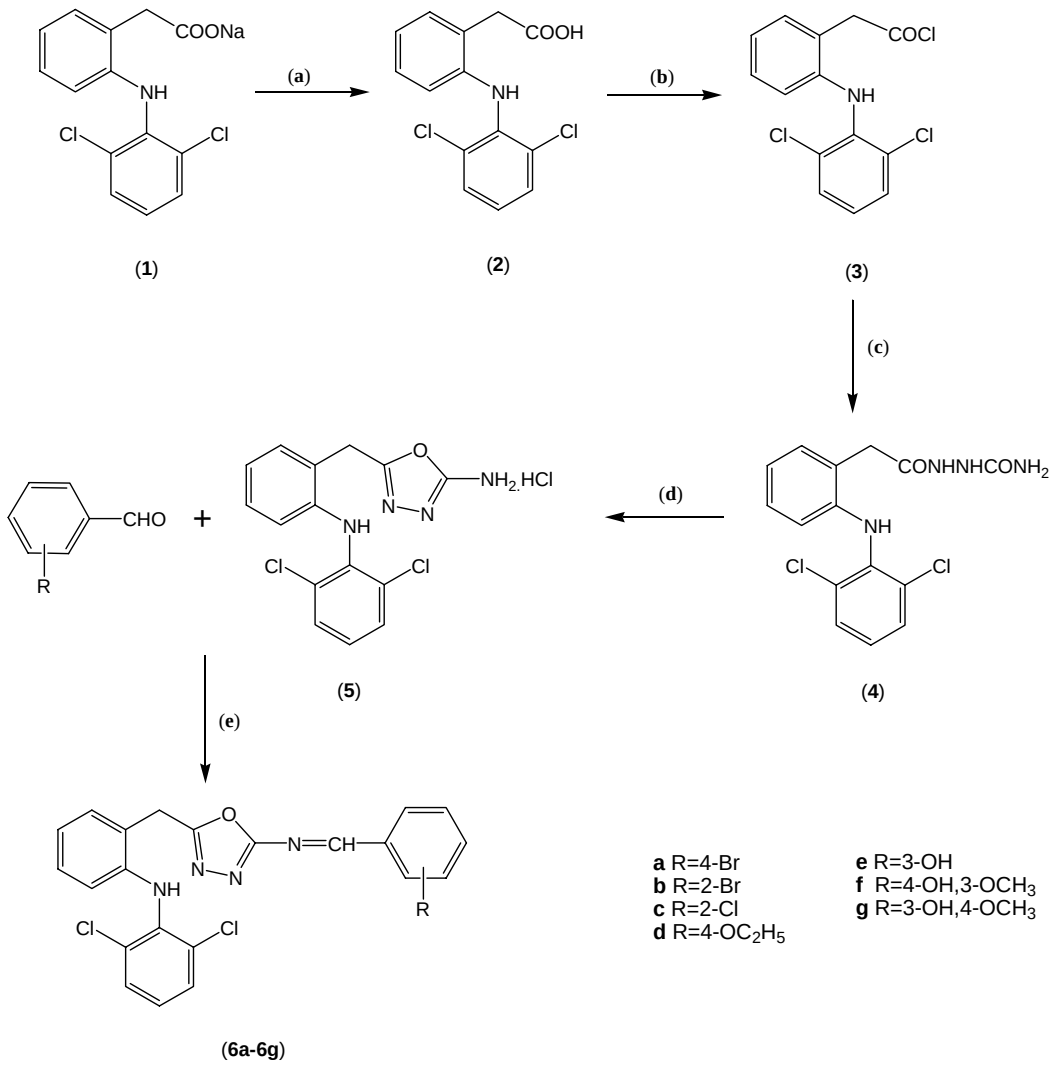
ABSTRACT

Inflammation is a tissue reaction to infection, injury, irritation etc. and is a part of host defense mechanism. Non-steroidal anti-inflammatory drugs (NSAIDs) are widely used for the treatment of pain, inflammation and arthritis. In 1971, Vane and coworkers made the landmark observation that NSAIDs acts by blocking generation of certain chemicals such as prostaglandins (PGs) by the enzyme cyclooxygenase (COX).

Diclofenac, an aryl-acetic acid derivative a non-steroidal anti-inflammatory (NSAID) drug inhibits PG synthesis. Sodium salt of diclofenac is one of the most frequently used NSAIDs worldwide (5 million prescriptions are filled yearly) and was approved in the US firstly in the year 1988. The presence of free carboxylic acid moiety in the diclofenac is mainly responsible for the associated side effects such as gastric ulceration. Several studies describes the derivatization of the carboxylate function of NSAIDs with less acidic azoles, viz. 1, 3, 4-oxadiazole, etc. which resulted in an increased anti-inflammatory activity with reduced ulcerogenicity.

Seven new hybrids of 1,3,4-oxadiazole and diclofenac acid was synthesized to decrease the side effects associated with the acidic function of diclofenac acid such as gastric ulceration to increase the anti-inflammatory activity (*Scheme-1*). The synthesized derivatives were evaluated for their anti-inflammatory & anti ulcer activity using various animal models. Among the synthesized derivatives, the compound **6c** was found to be most active as compared to the standard diclofenac sodium.

Keywords: NSAIDs, Cyclooxygenase, Diclofenac acid, 1,3,4-Oxadiazole



Scheme-1: Reagents and conditions : (a) Distt. H_2O, Conc. HCl, (b) $SOCl_2$, (c) Semicarbazide salt, NaOH, Methanol, (d) I_2/KI,NaOH, Methanol, (e) Methanol/ Acetic acid, NaOH

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