

Design and Synthesis of Some Quinazoline Derivatives as Anti-Inflammatory Agents

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ABSTRACT

Inflammation is the response of immune system towards injury and infection. It is divided into two main categories acute and chronic. Acute inflammation occurs rapidly within few hours after injury and infection and causes acute bronchitis, infected ingrown toenail, sore throat whereas chronic inflammation occurs from unresolved or recurrent acute inflammation leading to asthma, chronic peptic ulcer, tuberculosis and rheumatoid arthritis. In the market, large number of anti-inflammatory drugs are available but unfortunately they all are associated with one or other side effects. Therefore, efforts are made towards the development of new molecules having potential anti-inflammatory activity with less side effects. In general, quinazoline derivatives are known to possess wide range of biological activities such as antibacterial, anti-inflammatory, analgesic, antitubercular, antifungal, antihypertensive and anticancer. The anti-inflammatory profile of the molecule depends upon the type and location of a specific substituent on quinazoline nucleus. Therefore, to overcome the problem of side effects like gastric ulcerogenic, a new class of 4-amino-quinazoline derivatives was synthesized and studied for anti-inflammatory activity.

KEYWORDS

Inflammation, quinazolines, anti-inflammatory agents

INTRODUCTION

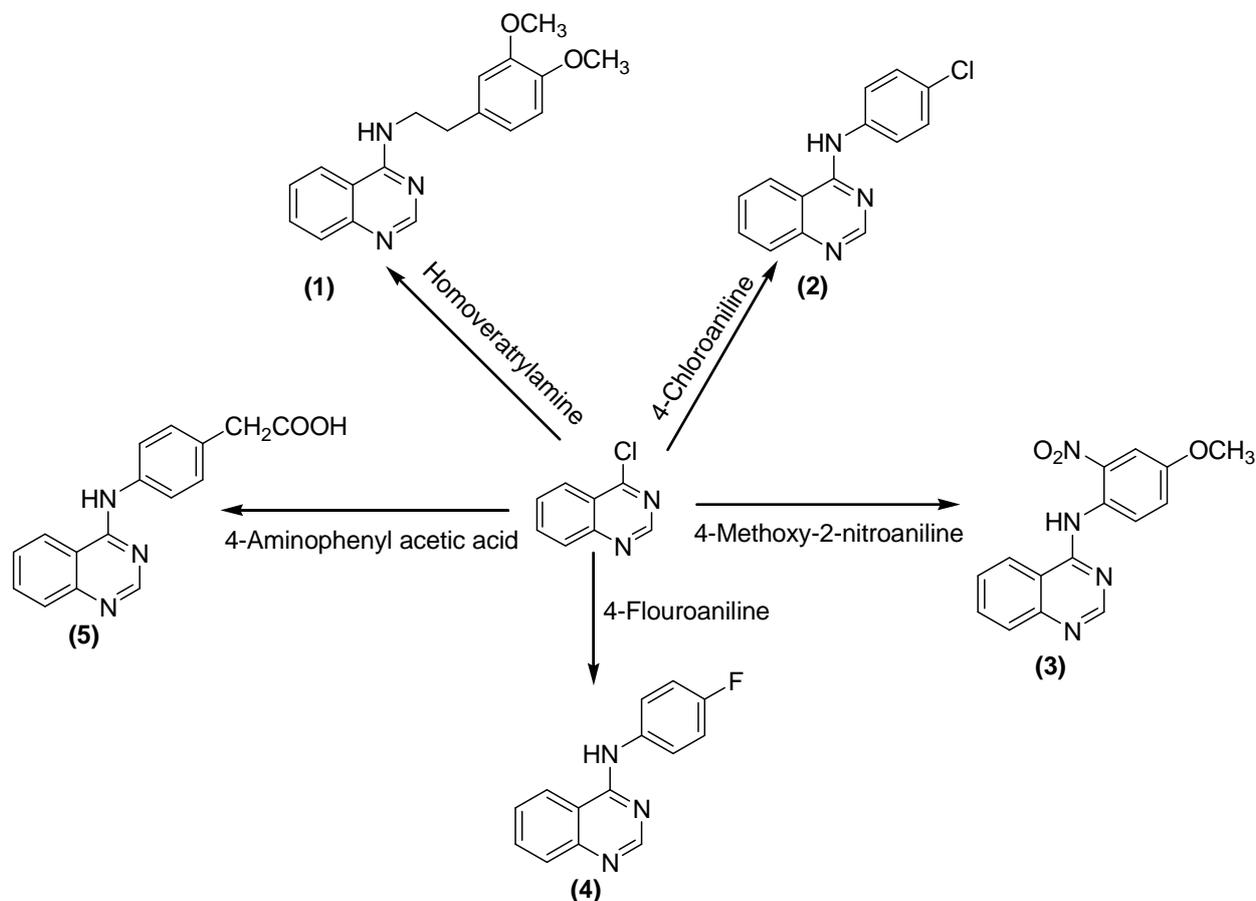
Inflammation is a local response of the living tissues subjected to trauma due to injury. Inflammation causes redness, heat, and pain. Quinazolinering system possess a wide range of biological activities including antibacterial, antitubercular, antifungal, antihypertensives, anti-inflammatory, anticancer, antifolate and analgesic. Quinazolines belong to category of non-steroidal anti-inflammatory agents. Five different aryl/alkyl amino substituents were introduced on quinazoline nucleus to yield potent anti-inflammatory agents.

EXPERIMENTAL METHODS

Synthesis of 4-aryl/alkyl amino substituted quinazolines: The NH spacer at 4-position between quinazoline and aryl nucleus was produced to obtain active chemical entities. The starting compound anthranilic acid was prepared by treating phthalimide with bromine and sodium hydroxide, cyclization of which gave quinazolin-4-(3H)-one. Further chlorination of the quinazolin-4-(3H)-one was done by heating under reflux with phosphorous oxychloride afforded 4-chloroquinazoline, which was substituted with different aryl/alkyl substituents to obtain the target 4-aminoquinazoline derivatives (**1-5**).

Anti-inflammatory Activity: The activity was conducted on Sprague Dawley rats by the carrageenan-induced rat paw edema model using Indomethacin as standard at 20mg/kg.

Scheme I



Scheme I: Synthesis of 4-aminoquinazoline derivatives

RESULTS AND DISCUSSION: The synthesized compounds were characterized by using various spectral techniques. The compound **4** produced anti-inflammatory activity comparable to the standard drug indomethacin (20mg/kg) without resulting in any ulcerogenic side effects.

CONCLUSION: Efforts have been made towards the development and identification of new molecules having potential anti-inflammatory activity with minimal side effects. The *N*-(4-fluorophenyl)-quinazolin-4-amine (**4**) was found to be the most potent derivative of the series. Fluorine atom on the phenyl ring at 4 position of quinazoline ring resulted in improvement in potency towards inflammation.

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