Conventional and Microwave Assisted Synthesis of 3-(Substituted)-2-phenyl quinazolin-4(3H)-one and their Antibacterial and Anthelmintic Activity

S. Debnath and S. Y. Manjunath  
Department of Pharmaceutical Chemistry, Srikrupa Institute of Pharmaceutical Sciences, Velkatta, Kondapak, Medak District, Siddipet, Andhra Pradesh 502 277, India.  
Received April 6, 2011; accepted June 6, 2011

ABSTRACT  
The present research work was aimed to synthesize a series of various substituted quinazolinone containing 3-(substituted)-2-phenylquinazolin-4(3H)-one. The compound 3-[(2-oxo-4-phenylazetidin-1-yl)-carbonyl]-2-phenylquinazolin-4(3H)-one, II was prepared by treating 4-oxo-2-phenyl-N-[(E)-phenylmethylidene]quinazoline-3(4H)-carboxamide, I with acetyl chloride and triethylamine (TEA) in benzene by conventional and microwave irradiation method. Synthesis of 3-[(2-oxo-3-(2,4-dichlorophenoxy)-4-phenylazetidin-carbonyl]-2-phenylquinazolin-4(3H)-one, III was carried out by reacting I with 2,4-dichlorophenoxyacetic acid and thionyl chloride in benzene. The compound 2-phenyl-3-(5-phenyl-1H-1,2,4-triazol-3-yl)quinazolin-4(3H)-one, IV was obtained by reacting I with hydrazine hydrate in ethanol. Synthesis of 2-phenyl-3-(5-phenyl-1,2,4-oxadiazol-3-yl)quinazolin-4(3H)-one, V was done by reacting I with hydroxylamine hydrochloride in ethanol. These derivatives were prepared by microwave as well as the conventional method. Structure of the compounds has been established by means of IR, $^1$H-NMR and MS. All the compounds were evaluated for antibacterial activity against Gram-positive bacteria like Staphylococcus aureus , Bacillus subtilis and Gram-negative bacteria like Pseudomonas aeruginosa, Escherichia coli. Most of the compounds showed significant antibacterial activities when compared with the standard drug ciprofloxacin at the concentration of 500 µg/ml and 250 µg/ml. In this research work, in vitro anthelmintic activity of 3-(substituted)-2-phenylquinazolin-4(3H)-one carried out in comparison with piperazine citrate. These newly synthesized quinazolinone derivatives showed paralysis and were followed by death at concentrations of 10 mg/ml for the screening of the anthelmintic activity.

KEYWORDS: Quinazolin-4(3H)-one; azetidinone; triazole and oxadiazole.

Introduction  
The objective of the present study was to develop 3–(substituted)-2-phenylquinazolin-4(3H)-one derivatives to search for the more potential safe antibacterial and anthelmintic drugs. Microwaves are electromagnetic radiations. Microwave energy is similar to that of infra red or ultra violet rays. The frequency of microwaves ranges from 300 MHz to 20 GHz (1-0.01 m wavelength). Microwaves represent a non-ionizing radiation that influences molecular motions such as ions migration or dipole rotations but it does not alter the molecular structure. The absorption of microwaves causes a very rapid increase of the temperature of reagents, solvents and products (Shi and Hwanh 2003).

It has been reported that quinazolinone azetidinone, triazole and oxadiazole are the biodynamic heterocyclic moieties. Several quinazolinone derivatives have also been reported to show significant antibacterial, antifungal, anticonvulsant and anti-inflammatory activities. The scientific literature reveals that this activity is due to presence of azetidinone, triazole and oxadiazole moieties in a molecule and change in activity depends on the nature of substituents (Singh et al., 2010). In light of above observations, it was thought worthwhile to synthesize some new substituted quinazolinone derivatives by microwave as well as conventional methods. Increasing problems of the development of resistance in helminths against anthelmintics have led to the screening of these quinazolinones for their anthelmintic activity. Development of resistance to most of the commercially available anthelmintics became a severe problem worldwide. The efficacy of quinazolinones has been judged on the basis of the loss of spontaneous movement and/or complete destruction of the worm in vitro studies.  

3-[(2-oxo-4-phenylazetidin-1-yl)-carbonyl]-2-phenyl quinazolin -4(3H)-one, II was prepared by treating 4-oxo-2-phenyl-N-[(E)-phenylmethylidene]quinazoline-3(4H)-carboxamide, I with acetyl chloride and TEA in benzene. The 3-[(2-oxo-3-(2,4-dichlorophenoxy)-4-phenylazetidin]-carbonyl]-2-phenylquinazolin-4(3H)-one, III was...