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RESEARCH ARTICLE

SYNTHETIC STUDIES ON NOVEL NITROQUINAZOLINONE ANALOGS WITH ANTIMICROBIAL POTENTIAL

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A novel series of 4-[2-(3-bromophenyl)-7-nitro-4-oxo-3,4-dihydro-3-quinazolinyl]benzoyl amino acids and di/tripeptides was synthesized using diisopropylcarbodiimide (DIPC) as the coupling agent and *N*-methylmorpholine (NMM) as the base. Structures of all the newly synthesized peptide analogs were elucidated using IR, $^{1}H/^{13}C$ NMR, MS spectral data and evaluated for antimicrobial potential against pathogenic microbes. Most of the compounds exhibited potent antifungal activity against pathogenic *Candida albicans* and dermatophytes, in comparison to reference compound. Good bioactivity was also seen against gram-negative bacteria for synthesized compounds.

Key words: Quinazolinones, 4-Nitroanthranilic acid, Peptide analogs, Coupling, Antifungal activity.

INTRODUCTION

Literature is enriched with several works on synthesis of potent quinazolinone and benzoic acid derivatives with diverse biological activities (de Moura *et al* 2004; Trusheva *et al* 2010; Wu *et al* 2010; Sharma *et al* 2011; Wu *et al* 2011) but very few reports have been yet received regarding peptide coupling of quinazolinones, although potent peptide analogs of aroylbenzoic acid, furoic acid, aryloxyacetic acid, coumarin, quinoxaline, benzothiophene, benzimidazole and imidazole are already reported (Poojary *et al* 2001; 2003; Himaja *et al* 2002; 2003; Dahiya and Pathak, 2006a; 2006b; 2006c; Dahiya *et al* 2006a; 2006b; Dahiya and Pathak, 2007; Dahiya and Kaur, 2007a; 2007b; 2008; Dahiya, 2008a, 2008b; Dahiya *et al* 2008a; 2008b; Dahiya and Kumar, 2008; Dahiya and Bansal, 2008; Dahiya *et al* 2010). Keeping in view the pharmacological potential of quinazolinone and benzoic acid derivatives, both moieties were coupled in single nucleus and further, in continuation of our work on synthesizing potent antimicrobial peptide analogs (Dahiya and Mourya, 2012), a novel series of 4-[2-(3-bromophenyl)-7-nitro-4-oxo-3,4-dihydro-3-quinazolinyl]benzoyl amino acids and peptides was synthesized to get bioactive agents with biological interest. 4-[2-(3-bromo phenyl)-7-nitro-4-oxo-3,4-dihydro-3-quinazolin--nyl]benzoic acid (**1**) was prepared by interaction of *p*-aminobenzoic acid and 2-(3-bromophenyl)-7-nitro-4*H*-3,1-benzoxazin-4-one, which was in turn prepared from the 4-nitro anthranilic acid and 3-bromobenzoyl chloride at 0-5 °C in presence of pyridine (Gao *et al* 2007). Dipeptides Boc-Pro-Pro-OMe, Boc-Try-His-OMe, Boc-His-Phe-OMe, were prepared from the corresponding Boc-amino acids and amino acid methyl ester hydrochlorides using the dicyclohexylcarbodiimide (DCC) and tri-ethylamine (TEA) in dichloromethane (DCM). Similarly, Boc-Phe-Ile-Pro-OMe and Boc-His-Tyr-His-OMe was prepared by coupling Boc-Phe/ Boc-His with Ile-Pro-OMe/Tyr-His-OMe in alkaline conditions. For coupling, di/tripeptide units were selected from pharmacologically active natural as well as synthetic cyclic polypeptides (Dahiya and Pathak, 2006d; Dahiya and Gautam, 2011).