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RESEARCH ARTICLE

# SOLUTION PHASE SYNTHESIS AND BIOEVALUATION OF CORDYHEPTAPEPTIDE B

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**A natural phenylalanine-rich cyclic peptide - cordyheptapeptide B was synthesized by coupling of *N*-methylated tetrapeptide and tripeptide units after proper deprotection at carboxyl and amino terminals followed by cyclization of linear heptapeptide fragment. Required tetrapeptide and tripeptide units were prepared by coupling of Boc-protected dipeptides *viz.* Boc-Phe-*N*(Me)Gly-OH and Boc-Leu-Ile-OH with respective dipeptide methyl ester Pro-*N*(Me)Phe-OMe and amino acid methyl ester hydrochloride *N*(Me)Phe-OMe·HCl. Cyclization of linear polypeptide unit was done by pentafluorophenyl ester method. The structure of synthesized cyclopeptide was elucidated by spectral as well as elemental analysis. The newly synthesized cyclopeptide was evaluated for its antimicrobial and cytotoxic potential, and found to exhibit potent cytotoxicity against *Dalton's lymphoma ascites* (DLA) and *Ehrlich's ascites carcinoma* (EAC) cell lines, in addition to good antidermatophyte activity against *Trichophyton mentagrophytes* and *Microsporum audouinii*. Moreover, cyclopeptide displayed moderate antimicrobial activity against gram negative bacteria *Pseudomonas aeruginosa* and *Klebsiella pneumonia*.**

**Key words:** *Cordyceps* sp, Cyclic heptapeptide, Peptide synthesis, Cytotoxicity, Pharmacological activity, Antibacterial activity.

## INTRODUCTION

Past literature has proved the ability of fungi, bacteria, higher plants and marine sponges to produce a wide spectrum of natural products with diverse bioactivities (Haritakun *et al* 2007; Kornsakulkarn *et al* 2009; Jia *et al* 2007; Ebaba *et al* 2010; Daly *et al* 2009). Among these, cyclic peptides with unique structures and wide biological profile, are emerged as vital organic structures which may overcome the problem of resistance towards conventional agents. A novel natural cyclopeptide, cordyheptapeptide B has been earlier, isolated from a fungal strain *Cordyceps* sp and the absolute configuration of the cordyheptapeptide B was indicated by chromatographic analysis of acid hydrolyzate (Isaka *et al* 2007). Keeping in view the biological potential of natural cyclopolypeptides (Dahiya and Pathak, 2006; Pathak and Dahiya, 2003) and in continuation of our efforts toward synthesizing natural cyclic peptides (Dahiya 2007a; 2007b; 2007c; 2008a; 2008b; 2008c; 2008d; Dahiya and Gautam, 2010a; 2010b; 2010c; 2011; Dahiya and Kaur, 2007; 2008; Dahiya and Kumar, 2007; 2008; Dahiya and Pathak, 2006; 2007a; 2007b; Dahiya and Sharma, 2008; Dahiya *et al* 2006; 2009a; 2009b; 2009c) this study was directed toward the synthesis of a novel *N*-methylated cyclic peptide cordyheptapeptide B. The synthesized cyclic heptapeptide was also evaluated for its antibacterial, antifungal and cytotoxic potential.

## MATERIALS AND METHODS

### *General experimental part*

Melting point was determined by open capillary method and is uncorrected. L-amino acids,