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Synthesis, Structure and Antitumor Activities of Tridecapeptide PSPP3 from *Papaver Somniferum* Pollen

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Abstract: Five analogs and five segments of the *Papavor Somniferum* pollen tridecapeptide PSPP3 were designed and synthesized by using solid-phase peptide synthesis method. Their inhibitive activities to human liver tumor cell Bel-7402 were assayed by MTT method and their secondary structures in solution were determined by CD spectra. The relationship of the structure and activity was discussed.

Keywords: Pollen peptide, anti-tumor activity, structure and activity.

Pollen plays a key role in the reproductive process of higher plant, which contains much important substance with different physiological activities, of which peptide and protein are important ones[1,2]. Pollen is still widely used as nutritive and healthful food in many countries[1]. In recent years, we have paid much attention to the studies on the isolation, structure characterization and synthesis of some oligopeptides from several kinds of pollens[3-5], and found that they had some activities of promoting immunity and restraining some cancer cell division[5-7].

In previous studies, we have found that the active peptides isolated from *Brassica campestris* and *Papaver somniferum* pollens have some similarities in the sequences[3-5]. They have many amino acid residues containing carboxamide groups in side-chains and some consecutive ones in N- or C-terminus. In present study, PSPP3 with inhibition to some tumor strains, obtained from *Papaver somniferum* pollen, was chosen as a leading peptide. In order to find effective anti-tumor agents and the relationship of structure and activity, firstly, five analogs PSPP31, PSPP32, PSPP33, PSPP36 and PSPP37 were designed by replacing one or more N and/or Q residue (s) with D and/or E, respectively, to find out whether carboxamide group (s) on side-chain are important to anti-tumor activities. Secondly, decapeptide segment PSPP34 with NQN deduction from N-terminus and its analog PSPP38, in which N and Q were replaced with D and E, respectively, were designed to elucidate whether these three N-terminal amino acid residues are responsible for anti-tumor activities. Heptapeptides PSPP39 and PSPP35 based on N- and C-terminals and the analog PSPP310 derived from the N-terminal heptapeptide were also designed for finding the active site. All designed peptides were synthesized by using SPPS method. Their sequences are given as follows.

PSPP3	NQNGSNPKTVKQA	PSPP36,	DEDGSDPKTVKEA
PSPP31,	DEDGSNPKTVKQA	PSPP37,	NQNGSDPKTVKEA
PSPP32,	DENGSNPKTVKQA	PSPP38,	GSDPKTVKEA
PSPP33,	NENGSNPKTVKQA	PSPP39,	NQNGSNP
PSPP34,	GSNPKTVKQA	PSPP310,	DEDGSNP
PSPP35,	PKTVKQA		

The conformations of all related peptides were studied by CD spectra. PSPP37 showed mainly β -turn conformation. The others showed β -sheet conformation. However, PSPP31, PSPP33 and PSPP34 showed partial β -turn conformation.

Anti-tumor activities of all synthetic peptides were assayed by determining the inhibitive percents to human liver tumor cell Bel-7402 strain with the tetrazolium salt MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide] method[8]. PSPP35, partial sequence in C-terminus of PSPP3, showed slightly higher activity than PSPP3. While segments PSPP39 and PSPP310 derived from N-terminus of PSPP3 showed lower activities than PSPP3. These indicated that the segment in C-terminus is important to anti-tumor activity. However, the segment in N-terminus is not important to activity. The activities of the segments PSPP34 and PSPP37 are higher than PSPP38, which showed almost the same activity to PSPP3[9]. It seems that residues N and Q in PSPP34 are favorable to activity. According to activities of all analogs, we found that replacing some of residues N and/or Q in middle and N-terminal of the PSPP3 with D and/or E led to increase activity. Considering of conformation, β -turn conformation seems to favour anti-tumor activity.

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