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Peptides & microwave-assisted solid-phase synthesis at 60 °C using low-priced and wastes-reducing conditions

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Peptides, including those with antimicrobial activity (AMPs), are widely studied macromolecules isolated from natural sources. AMPs have been reported as promising candidates for the development of new drugs able to kill microorganisms pathogenic to humans [1]. Isolated and identified, these bioactive peptides are frequently synthesized in laboratory and the synthetics are used in research, therapeutics, animal feed & nutrition, veterinary, agriculture, environmental chemistry and cosmetics. Solid-phase chemical method (SPPS) is the most preferred method to produce synthetic peptides owing to its efficiency, speed, broadness and possibility of automation. Nevertheless, when the target peptide is long, chemically complex, cyclic, specifically modified and/or prone to aggregation, SPPS can be become sluggish, very expensive and a rich source of contaminants or environmentally unsafe wastes. Aiming to help avoiding or minimizing these drawbacks, in previous studies we established reaction conditions of reduced costs, reaction times, side-reactions and wastes for all steps of SPPS [2-4]. Here, we describe the results of an original study elegantly designed to validate the usefulness of our conditions for total synthesis of a long aggregating glycine-rich AMP, the C-terminal amidated portion of acanthoscurrin. The success achieved using CLEAR amide resin, 60°C, conventional heating or microwaves, no amide backbone protection, no chlorinated solvents and FT-Raman spectroscopy for monitoring peptide assembly on the polymeric resin further support routine use of low excess of N-acylated amino acids, 60°C, microwaves and solvents greener than those used in traditional SPPS (at room temperature). This combination is especially advantageous for peptide chemists working in countries that do not manufacture most items required for SPPS (amino acid derivatives, coupling reagents, resins, some solvents, vials and equipments), so synthetic peptide chemistry can be limited by the high costs, regulations, delays and risks of importation.

Key-words: peptides, peptide-resins, synthesis at high temperature, peptide synthesis
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