

# Structure–activity relationships of $\alpha_s$ -casein peptides with multifunctional biological activities

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**Abstract** Multifunctional bioactive peptides have a wider role in modulating physiological functions and possess multiple biological activities. Peptides from bovine milk with sequences QKALNEINQF [p10] and TKKTKLTEEEKNRL [p14] from  $\alpha_{s2}$  casein f (79–88) and  $\alpha_{s2}$  casein f (148–161) were identified to be having multifunctional biological activities and were synthesized. These synthesized peptides show various biological activities like angiotensin-converting enzyme inhibition, prolyl endopeptidase inhibition, antioxidant, and antimicrobial activities. The mode of antimicrobial mechanism was studied and p10 shows depolarization of cell membrane, whereas p14 was found to display DNA-binding activity. Structural studies envisaged backbone flexibility, for differences in their mode of action. Peptide structure function studies were correlated to understand their multifunctional biological activity.

**Keywords** Peptides · Casein · Multifunctional · Circular dichroism · DNA binding · Antiulcer · Antihypertensive · Antimicrobial

## Abbreviations

ACE	Angiotensin-converting enzyme inhibition
PEP	Prolyl endopeptidase
DNA	Deoxyribonucleic acid
CD	Circular dichroism
TFA	Trifluoroacetic acid
DPPH	2,2-Diphenyl-1-picrylhydrazyl
DiBAC <sub>4</sub> (3)	Bis-(1,3-dibutylbarbituric acid)trimethine oxonol

## Introduction

Milk is a complex mixture of proteins that provides the sole nutrient requirements to newborns. Milk contains proteins and encrypted biologically active peptides, which are released upon hydrolysis [1]. Bioactive peptides can affect numerous physiological functions of an organism. Once they are released in the body, they modulate various regulatory processes in the living cells as in the case of angiotensin-converting enzyme (ACE) inhibitory peptides, opioid peptides, antimicrobial peptides, mineral-binding peptides, immunomodulatory peptides, and cytomodulatory peptides [2, 3]. Since such peptides with biological activity are small in size, screening methods for their biological activity can be easily optimized and their therapeutic potential can be quickly investigated.

Peptides from cow's milk are multifunctional, i.e., they have more than one biological activity. Bioactive peptides are functional foods with health modulating benefits [4, 5]. Biologically active peptides have previously been identified and studied from in vitro enzymatic digests, in vivo gastrointestinal digests, and or by chemical synthesis [6]. Various bioactive peptides from bovine milk  $\alpha$ -casein have been structurally characterized and reported in literature [7–9].

Antimicrobial activity has a special role among the various characteristics pertaining to peptides. Antimicrobial peptides are widely distributed in nature and have been characterized both from entire animal and plant kingdoms [10, 11]. Antimicrobial peptides reported in literature function by permeabilizing cell membranes and inhibit DNA, RNA, and/or protein biosynthesis [12]. These peptides are more potent compared to synthetic antibiotics, and are less prone to resistance [13, 14].

The biological activity of peptides can be related to their conformation, hydrophobicity, propensity to form different

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