

## Application of Nisin in Food and Pharmaceutical Industries

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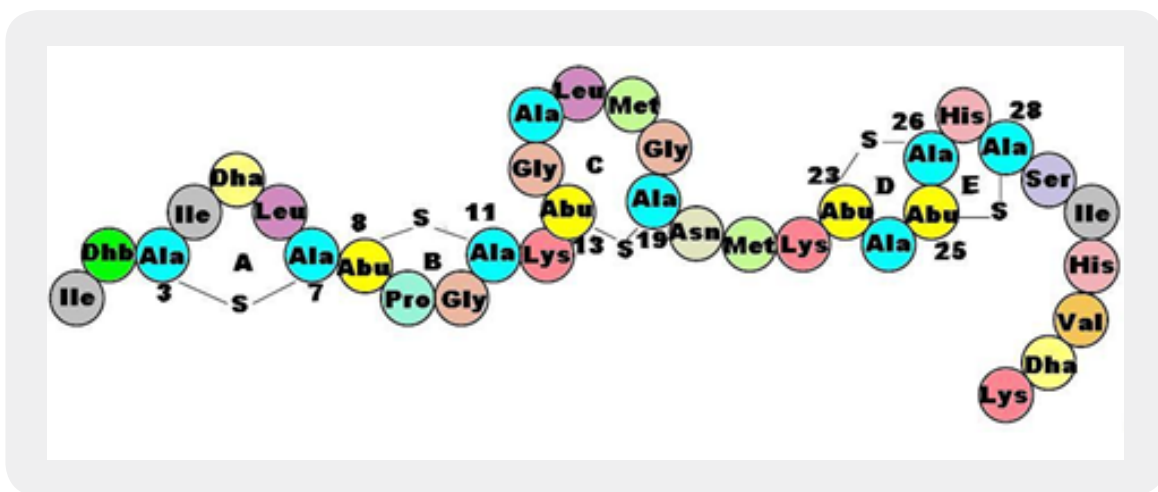
**Keywords:** *Nisin; Food and Pharmaceutical Industries; Staphylococcus Aureus; Gastric Cancer Cell*

### Abstract

In the present study, the potential of the antimicrobial peptide of nisin has been studied in the food (antibacterial activity) and pharmaceutical (anticancer activity) industries. This peptide can be used both as a preservative and as a drug because the formation of pore in the membrane of bacteria. In this study, the antimicrobial activity of nisin on reference strain of *Staphylococcus aureus* ATCC 2592, a food pathogen, and the effect of this peptide on the gastric cancer cell line (AGS) has been investigated. The effect of nisin on *Staphylococcus aureus* ATCC 2592 was studied by the MIC method and it was observed that nisin has an antibacterial effect on this bacterial strain. Study on cytotoxicity effect of nisin in different concentrations on the gastric cancer cell line showed that with increased concentration and treatment time, more cytotoxicity was observed.

## Introduction

Bacteriocins are ribosomal peptides that produced by lactic acid bacteria; these peptides, with antimicrobial activity, are acid and heat resistance and easy to digest. According to the Kaiser and Montville theory, bacteriocins should have two properties: 1) Protein nature. 2) non-cytotoxic on cells that produce them [1]. Lantibiotics are a class of bacteriosins that are small and heat-resistant peptides and they have lantionone and methyl lanthanide amino acids in their structures. A subgroup of lantibiotics is an elongated, flexible, and positively charged peptide that creat pores in the membrane of target bacterial species, such as nisin [2]. Nisin have 34 amino acids {C<sub>143</sub> H<sub>230</sub> N<sub>42</sub> O<sub>3</sub>} (Fig. 1); it has amphipathic structure with +4 charge, the N-terminal of this peptide is more hydrophobic than the C-terminal and produced by *Lactococcus lactis* bacteria; Nisin have antimicrobial activity against a wide range of gram-positive bacteria, including *Listeria monocytogenes* and spore-producing bacteria such as *Clostridium* and *Bacillus*. Nisin creating pores in the membrane of bacteria and breaking the ionic gradient and result the death of the bacterial cell [3, 4], in addition it is preventing the cellular biosynthesis [5]. Because of the non-toxicity of this peptide, in 1969, FAO (Food and Agriculture Organization) and WHO (World Health Organization) allowed it to be used as a food preservative [6]. Many studies have been done on nisin in the pharmaceutical and food industries [7, 8, 9, 10]. In this study, we have evaluated the anticancer (in the pharmaceutical industry) and antibacterial (in the food industry) effects of nisin.



*Fig. 1. Nisin Structure.*

## Materials and Methods

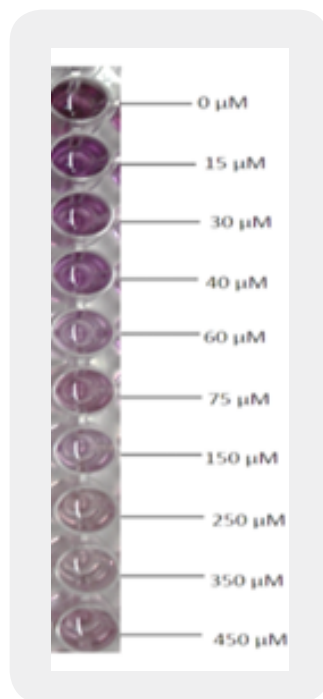
In order to prepare the nisin solution, the nisapline commercial powder was obtained from the Merck company (Germany), *Staphylococcus aureus* ATCC 2592 bacterial strain were purchased from the Iranian Scientific and Industrial Research Center. The gastric cancer cell line (AGS) was purchased from the Pastor Institute of Iran.

### Application of Nisin in Food Industry

One of the pathogenic bacteria in the food industry is *Staphylococcus aureus*, which is responsible for many food poisonings. To evaluate the antibacterial effect of nisin on this bacterial strain, minimum inhibitory concentration (MIC) method was used. For this purpose, micro-broth dilution method was used at concentrations of 1 to 4 mg/mL of nisin at 24, 48 and 72 hours. A well of bacteria without any treatment was considered as control.

### Application of Nisin in Drug Industry

Gastric cancer is one of the most common cancers in the world and the fourth common cancer and the second deadly cancer in the world [11]. In order to study the cytotoxic effects of nisin on AGS cell line, these cells were cultured in  $1 \times 10^4$  cells in 96 well plates and incubated for one day at incubator at 37°C, after 24 hours, these cells were studied by MTT method with different concentrations of 15–450 micromolar of nisin for 3 times each repeat concentration at 24, 48 and 72 hours (Fig. 2). Finally, the cytotoxic effect of nisin on AGS cell was studied as mentioned in previous paper [12].



**Fig. 2.** Comparison of the MTT assay for different levels of nisin. The greater the color intensity is, the greater the number of live cells is.

### Results

The MIC of nisin on *Staphylococcus aureus* ATCC 2592 was determined 2.5mg/mL by micro-broth dilution method. With increasing concentration and treatment time by nisin the viability of AGS cell line were decreased, IC50 value was determined 62μM after 72 hours [12].

## Discussions

*Staphylococcus aureus* is a gram-positive and spherical bacterium. Toxin-related diseases of these bacterium include skin flashing syndrome, food poisoning, toxic shock, and acute infections of this bacterium, ulcers, bacteremia, endocarditis, pneumonia, infectious arthritis. Gastrointestinal cancers associated with hereditary and environmental factors have high worldwide prevalence [13,14]. Almost 50% of the gastrointestinal cancers are related to gastric cancer. According to the results of the antimicrobial effects of nisin on *Staphylococcus aureus* ATCC 2592 bacteria and many other bacterial strains, as well as non-toxicity and its degradation by digestive enzymes, nisin can be considered as an effective peptide in the food industry against foodborne pathogens. Because of recent research on the anticancer effects of this peptide on many cancer cell lines, including head and neck squamous cell carcinoma (HNSCC) cancer cells, skin carcinogenesis, HaCaT cell lines, T cells, nisin can be considered as a peptide with therapeutic effects in the field of pharmaceutical sciences.

## Conclusions

Nisin is a natural peptide that has many abilities in various industries, including the pharmaceutical and food industries. Because of the non-toxicity of this peptide, this peptide is suggested to be studied in various fields.

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## Conflicts of Interests

All authors have read and approved this version of the article and we have no conflicts of interest.

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