

Secretariat,
Codex Alimentarius Commission, Joint
FAO/WHO Food Standards Programme
Viale delle Terme di Caracalla
00153 Rome, Italy

Dear members of Secretariat!

According to the evidence of scientific data nisin (INS 234) is lantibiotic (bacteriocin) produced by *Lactococcus lactis* subsp. *Lactis*. (Lantibiotics are a class of peptide antibiotics (bacteriocine) that contain the characteristic polycyclic amino acids lanthionine or methyllanthionine, as well as the unsaturated amino acids dehydroalanine and 2-aminoisobutyric acid).

These proposals of CCFA 47 according nisin using in dairy products, fine bakery wares and heat-treated meat products are based on the conclusion of JECFA about safety of nisin (WHO FOOD ADDITIVES. SERIES:68). However, in our opinion, JECFA have taken in consideration (as a base) the safety of nisin as chemical substance, but did not take into account its biological effects.

As a result of highly biological activities, have been showed that bioengineered lantibiotic nisin can potentially be employed as novel anti-microbials preparation to combat medically significant bacteria and their multi-drug resistant forms of *Clostridium difficile*, *Mycobacteria tuberculosis* (H37Ra), *M. kansasii* (CIT11/06), *M. avium* subsp. *hominissuis* (CIT05/03) and *M. avium* subsp. *paratuberculosis* (MAP) (ATCC 19698) [BMC Microbiology 2013, P.13:23; Bioengineered Bugs, 2010, Vol.1:6, P.408-412]. However according to established principles medicaments used in clinic cannot be used in food industry. Obtained data can be a rational for nisin excluding from the list of approved food additives.

It is showed that nisin could be inhibitor of lactobacterium growth which is the most important part of normal gut microbiota. For example, nisin could inhibit a growth of *Lactobacillus gasseri* in concentration of 25 ng/ml [Applied and Environmental Microbiology, 2013, Vol.79, N 10, p. 3160–3170]. As a result this process can inhibited the immunity status of population. Antimicrobial peptides play a significant role in building an innate immunity [Applied and Environmental Microbiology, 2013, Vol.79, N 10, p. 3160–3170; Drugs, 2003, Vol. 63, P.389–406]. Obtained data about mechanisms of resistance of *Staphylococcus aureus*, *Streptococcus bovis*, *Listeria monocytogenes*, *Clostridium botulinum* and *Bacillus subtilis* into nisin [Applied and Environmental Microbiology, Feb. 2001, p. 808–813; Applied and Environmental Microbiology, 2013, Vol. 79 N 18 p. 5682–5688; Applied and Environmental Microbiology, 2012, Vol. 78, N 8, p. 2923–2929; Applied and Environmental Microbiology, Feb. 1999, p. 659–664; Mol Microbiol., 2013 November, Vol. 90(3), P. 502–518].

The possibility of nisin influence on the activity of specific bacterial enzymes (α - and β -glucosidases, α -galactosidases and β -glucuronidase) in crop, ileum and caeca was taken for the justification of its use in case of chicken breed [PLOS ONE, www.plosone.org, December 2013, Vol. 8, Is.12].

In proposed by CCFA 47 data there are only arguments in favor of nisin based on its technology justification. However it should be mentioned that the higher level of nisin influence at the growth of pathogenic and potentially pathogenic microorganisms define it as substance with higher level of biological activity. For another thing, violation of hygienic regulations cannot be the justification of the food additive use (Citation: “Nisin is an extremely important preservative for use in meats, particularly in warm climates or in developing nations where access to stable refrigeration may be limited”, Agenda Item 5(e) CX/FA 15/47/11 Add.1., Nisin Background»). The storage of food with short life-cycle without refrigerators is impossible.

In our opinion the proposals according using of nisin (INS 234) in the different food categories (01.4.4, 01.6, 01.6.1, 01.7, 07.2, 08.2.2, 08.3.2, 08.4) provided in Agenda Item 5(e) CCFA 47 cannot be accepted before risk estimation and risk assessment of this food additive.

The Contact Point of Codex Alimentarius in Russian Federation,
Director of Institute of Nutrition,
Dr. of medicine science, Professor, Academic of Russian Academy of Science

Victor A. Tutelyan

Prepared by: S. Hotimchenko
O. Bagryantseva
G. Shatrov
S. Sheveleva
L. Minaeva