

A simple and sensitive LC-MS/MS method for determining residues of the tranquilizer chlorpromazine in livestock products, seafood, and honey

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Hiroyuki Kikuchi, Takatoshi Sakai, Tomoko Okura, Satoru Nemoto, Hiroshi Akiyama

Division of Foods, National Institute of Health Sciences

Abstract

A simple and sensitive analytical method for determining residues of the tranquilizer chlorpromazine in foods such as livestock products, seafood, and honey was developed. The method involves solvent extraction with acetone, clean-up using InertSep MC-1 strong cation-exchange solid-phase extraction cartridges, and liquid chromatography–tandem mass spectrometry (LC-MS/MS) analysis with selective reaction monitoring in positive ionization mode. Because chlorpromazine was gradually degraded in the extraction step when using methanol or ethanol as the extraction solvent, we examined the stability of chlorpromazine in the presence of various solvents. Acetone was selected as the extraction solvent because chlorpromazine was not degraded over time in acetone extracts. Because chlorpromazine adsorbs onto glass surfaces, polypropylene tubes were used for the extraction step to prevent loss of the recovery. The developed method was validated using eight food products spiked with chlorpromazine at 0.1 µg/kg. The validation results exhibited excellent recovery (range, 86-106%) and precision (variation <10%). The limit of quantification (S/N ≥10) of the developed method was 0.1 µg/kg. The proposed method would be very useful for regulatory monitoring of the illegal use of chlorpromazine in foods.

Keywords : chlorpromazine, livestock products, honey, seafood, LC-MS/MS

I Introduction

Chlorpromazine (CPMZ), a tranquilizing and anti-emetic agent of the phenothiazine group (Fig. 1), is a first-generation antipsychotic drug that was introduced into clinical use globally in the 1950s. The antipsychotic effect of CPMZ derives from its activity as an antagonist of many cell membrane receptors, notably those for dopamine,

noradrenaline, serotonin, and norepinephrine¹⁾. CPMZ has been used in livestock such as cattle, swine, sheep, and goats to prevent mortality and to reduce meat quality degradation during transportation to the slaughterhouse. Although the hydrochloride is distributed in Japan as an antipsychotic drug to treat schizophrenia under the trade name Contomin, its use in food-producing animals is prohibited²⁾.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) was unable to establish an acceptable daily intake level for CPMZ due to a lack of relevant toxicologic data, the long-term persistence of CPMZ in humans, and the drug's broad spectrum of additional effects²⁾. The JECFA thus recommended against the use of CPMZ in food-producing animals. Therefore, the use of CPMZ in livestock animals is prohibited in Japan, the European Union, and the USA, and a maximum residue limit (MRL) for CPMZ in food has not been established. Illegal use of CPMZ in food-producing animals increases the possibility of residues remaining in livestock

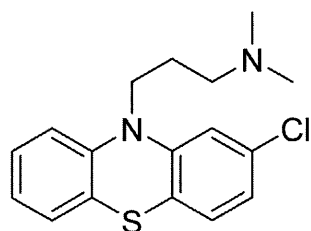


Fig. 1. Chemical structure of chlorpromazine