Dispersive Liquid-Liquid Microextraction Combined with Field-Amplified Sample Stacking in Capillary Electrophoresis for The Determination of Non-Steroidal Anti-Inflammatory Drugs in Milk and Dairy Products

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Non-steroidal anti-inflammatory drugs (NSAIDs), including etodolac (ET), naproxen (NAX), ketoprofen (KTP), furbiprofen (FBP) and diclofenac (DIC), are one of the most frequently used pharmaceutically active compounds in veterinary medicine [1]. Their effectiveness in reducing pain and preventing inflammation has resulted in their widespread use in food-producing animals [2]. These uses, however, are not without side effects which include gastrointestinal bleeding, intestinal ulceration, aplastic anaemia and inhibition of platelet aggregation [3]. As such, the use of NSAIDs in food-producing animals might create public health problems. In order to monitor their levels and to set legislations, sensitive and efficient analytical methods are urgently in need.

A simple and cost-effective sample preconcentration method using dispersive liquid-liquid microextraction (DLLME) [4] was developed for the determination of the aforementioned five NSAIDs. Using salting-out extraction, NSAIDs were efficiently extracted from the aqueous sample solution into an organic solvent (acetonitrile) phase. Two milliliters of the acetonitrile layer (disperser solvent) were mixed with 150 µL of chloroform (extraction solvent) and the mixture was rapidly injected into 8.0 mL deionized water. An emulsion formed due to the dispersion of fine droplets of the extraction solvent into the sample solution. After centrifugation, the fine droplets of chloroform containing the enriched analytes sedimented, were separated and back-extracted into 70 µL aqueous solution (at pH 11.3) for direct injection into capillary electrophoresis (CE). Parameters affecting extraction efficiency, including pH and volume of sample and back-extraction solutions, type and volume of extraction and disperser solvents, ionic strength as well as extraction time were systematically studied and optimized. In order to enhance the sensitivity of CE further, the online preconcentration technique of field-amplified sample stacking (FASS) [5] was applied.

Under optimum extraction and stacking conditions, enrichment factors of 46-230 as compared to conventional capillary zone electrophoresis (CZE) were obtained resulting in limits of detection (LOD) of 3.0-13.1 µg kg⁻¹ with DLLME-FASS-CE. Calibration graphs showed good linearity in the range of 10.0-5000 µg kg⁻¹ with coefficients of determination (R²) in the range of 0.9915-0.9997 and relative standard deviations (RSD %) of the analyses less than 6.2% for (n = 5). The proposed method was applied to the analysis of fresh (unpasteurized) and bottled (pasteurized) bovine milk, yogurt, as well as white cheese samples with relative recoveries in the range of 87.0-102 %. The results showed that the proposed method was a rapid and convenient method for the determination of NSAIDs in milk and dairy products.

KEYWORDS: capillary electrophoresis, dairy products, dispersive liquid-liquid microextraction, milk, non-steroidal anti-inflammatory drugs

REFERENCES: