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European Journal of Applied Engineering and Scientific Research, 2020, Volume 9 issue 2

ISSN: 2278-0041

Analysis of isotretinoin and its metabolites by capillary electrophoresis with on-line preconcentration Technique

Ying-Xuan Huang and Yen-Ling Chen

Kaosiung Medical University, Taiwan.

Abstract:

The reasons for acne formation are as follow: testosterone converted into dihydrotestosterone (DHT), and DHT combines with androgen receptors simultaneously. When hair follicle is clogged, sebaceous gland cells are stimulated to produce certain amounts of sebum. It causes the propionibacterium acnes to proliferate, which secrete lipase that goes on to decompose sebum into free fatty acid, and lead to inflammation. Isotretinoin is one of the acne therapeutic drugs which reduce acne formation by binding to the retinoid receptor. According to the literature study, the dosage of isotretinoin correlates with its adverse effects, such as dryness of the skin and mucosa, conjunctivitis, night blindness, etc. Therefore, it's desirable to develop an analytical method to detect and evaluate the concentrations of isotretinoin and its metabolites tretinoin, 4-oxo-isotretinoin. In this study, capillary electrophoresis with low solvent and sample consumption was chosen as the analytical instrument. The application of on-line pre-concentration technique can be used to enhance the sensitivity.

Introduction:

Mycotoxins are natural secondary metabolites produced by filamentous fungi (Aspergillus, Fusarium, and Penicillium). They mainly include aflatoxins (AFs), trichothecenes, fumonisins, ochratoxin A (OTA), patulin (PAT) and zearalenone (ZEA) [1–3]. Nowadays, about 500 mycotoxins are currently known, and they contaminate almost 40% of cereals globally produced [4]. In addition to the known mycotoxins, there are also the so called "emerging mycotoxins", which refer to those fungal metabolites that could be toxic, which we have no control of and or restrictions against [5,6]. Non-regulated mycotoxins constitute a very important issue as their toxicity is not known [6]. The number of these mycotoxins is very alarming, as confirmed by a recent study on different maize samples from Serbia, which pointed out the presence of more than one hundred nonregulated fungal metabolites in samples cultivated over four years [6,7]. Mycotoxins represent dangerous contaminants of agricultural products and foodstuffs (mainly cereal products, fruits, vegetables, and derived products, such as wine and juices) and toxicological agents for animal and human health [3,8]. Their riskiness is related to their high stability over time, also at high temperatures [3]. Their toxicity concerns teratogenic and/or mutagenic effects, and some of them (aflatoxin B1- AFB1, aflatoxin M1-AFM1, OTA) are human carcinogens [1,2,4,9]. Others, such as ZEA, exhibit carcinogenic, hematotoxic, and hepatotoxic properties only in in vitro experiments and in some animal species [2,3,9]. They can also cause immunosuppression and hormonal disorders [2,9]. In addition, the few works on mycotoxins in pet food showed their high toxicity in relation to pets' health [10]. The main issue regarding human toxicity is correlated to animal toxicity. In fact, AFs, OTA, ZEA, ergot alkaloids, and fumonisins were particularly toxic for farm animals, mainly non-ruminants and

Note: This abstract is received at the 8th Annual Congress on Analytical and Bio analytical Techniques which was in the August 28-30, 2017 at Brussels, Belgium.

cereal grains or forages remain the principal food source which can affect animal and human health [9]. Considering their abundance and toxicity, a careful evaluation of risk assessments has caused the European Commission (EC) to adopt restricted regulations to control their limits in foodstuffs [1,11–13] with specific official methods [12]. The control of food and feed is fundamental during production and storage phases [4]. Standardized methods for determination of different mycotoxins in many food matrices mainly consist of Thin-Layer Chromatography (TLC) and HighPerformance Liquid Chromatography (HPLC) [14]. The methods must guarantee the determination and quantification of trace levels of mycotoxins in complex food matrices and biological samples, as mycotoxins are mainly produced in a very low concentration [1]. Another great challenge in mycotoxin analysis is related to the fact that a single filamentous fungus can produce many different mycotoxins, so it is necessary to have rapid multi-analytemethods[15].

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