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Review

Analytical methods for the assessment of endocrine disrupting chemical exposure during human fetal and lactation stages: A review

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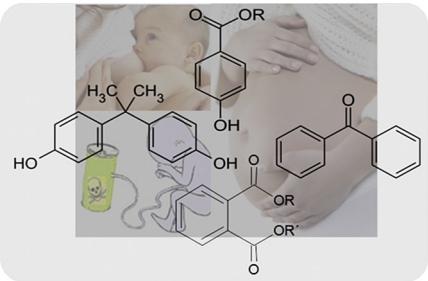
HIGHLIGHTS

- A review of analytical methods for the assessment of EDCs exposure during the first stages of the human life is developed.
- Placenta, cord blood, meconium, amniotic fluid, breast milk, blood and urine are the studied samples.
- The work is focused on four EDCs families: BPA, phthalates, UV-filters and parabens.
- The work mainly focused on sample preparation and the analytical techniques used.
- Assessment of exposure to EDCs during first stages of life will help to prevent future health issues.

GRAPHICAL ABSTRACT



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ABSTRACT

In the present work, a review of the analytical methods developed in the last 15 years for the determination of endocrine disrupting chemicals (EDCs) in human samples related with children, including placenta, cord blood, amniotic fluid, maternal blood, maternal urine and breast milk, is proposed. Children are highly vulnerable to toxic chemicals in the environment. Among these environmental contaminants to which children are at risk of exposure are EDCs —substances able to alter the normal hormone function of wildlife and humans—. The work focuses mainly on sample preparation and instrumental techniques used for the detection and quantification of the analytes. The sample preparation techniques include, not only liquid–liquid extraction (LLE) and solid-phase extraction (SPE), but also modern microextraction techniques such as extraction with molecular imprinted polymers (MIPs), stir-bar sorptive extraction (SBSE), hollow-fiber liquid-phase microextraction (HF-LPME), dispersive liquid–liquid microextraction (DLLME), matrix solid phase dispersion (MSPD) or ultrasound-assisted extraction (UAE), which are becoming alternatives in the analysis of human samples. Most studies focus on minimizing the number of steps and using the lowest solvent amounts in the sample treatment. The usual instrumental techniques employed include liquid chromatography (LC), gas chromatography

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(GC) mainly coupled to tandem mass spectrometry. Multiresidue methods are being developed for the determination of several families of EDCs with one extraction step and limited sample preparation.

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1. Introduction

Endocrine disrupting chemicals (EDCs) are a group of natural and synthetic chemicals that may interfere with the normal function of the endocrine system in animals and humans [1]. EDCs can act during fetal development, infancy, early childhood, puberty, adulthood and old age. In humans, the timing of EDC action often determines the strength of the impact. In adults the EDC has an effect when it is present, but when the EDC is withdrawn, the effect diminishes [2]. In contrast, exposure to EDCs during development (*in utero*, infancy and early childhood) can have permanent effects if the exposure occurs during the period when a specific tissue is developing. These effects may only become visible decades later. This is called “developmental programming” [3].

Hormones control the normal development of tissues from the fertilized sperm and egg to the fully developed fetus. Since some tissues continue developing after birth —like the brain and reproductive system— the sensitive period for these tissues is extended, sometimes for decades after birth. When a tissue is developing, it is more sensitive to the action of hormones and thus EDCs. Moreover, children's metabolic pathways, especially in the first months after birth, are immature. This means that children's ability to metabolize and excrete EDCs is lower than that of adults', making them more vulnerable to these chemicals [4].

The mechanisms through which EDC exposure during development can alter the development of specific tissues, leading to increased susceptibility to diseases later in life, are just beginning to be understood. It is clear that hormones play an important role in cell differentiation, which leads to the development of tissues and organs. Once tissues and organs are fully developed and active, then hormones have a different role: to control the integration of signals between tissues and organ systems and to maintain normal function. Early development (when hormones are controlling cell changes to form tissues and organs) is thus a very sensitive time frame for EDCs action. If an EDC is present during the developmental programming of a tissue, it could disrupt the normal hormone levels, leading to changes in tissue development-changes that would be stable across the lifetime and possibly confer sensitivity to disease later in life. These effects are not likely to be evident at birth, but may show up only later in life, from a few months to decades later [1]. The most prominent and well documented health concerns from exposure to endocrine disruptors are reproductive and developmental effects. Some of the disorders that have been seen in animal studies include oligospermia (low sperm count), testicular cancer, and prostate hyperplasia in adult males; vaginal adenocarcinoma, disorders of ovulation, breast cancer, and uterine fibroids in adult females. Disruption to thyroid functions, obesity, bone metabolism and diabetes are also linked to exposure endocrine disruptors [5–10].

In addition, children have greater exposure to EDCs for their body weight than adults. Children inhale four times more air, consume between six to eight times more calories and drink fourteen times more water per kilogram than an average adult. These differences result in children being exposed to greater burden of toxic chemicals from air, food and water [11].

Besides some naturally occurring compounds (lignans, coumestans, isoflavones, mycotoxins), numerous synthetic chemicals like bisphenol A (BPA) and its chlorinated derivatives, phthalates, organic UV-filters and parabens (PBs) have been implicated in endocrine disruption. The widespread use of these compounds and their potential risk to human health, have prompted interest in assessing human exposure [1,12–20], with special attention to children's exposure. Exposure may occur through inhalation, dermal contact or ingestion [1,11,12,18] and the metabolism may differ depending upon the exposure route and specific chemical structure characteristics [4,21,22]. Xenobiotics metabolism in humans is often divided into three phases: modification (phase I), conjugation (phase II), and further modification and excretion (phase III). These reactions act in concert to detoxify and remove these compounds from cells. In phase I, a variety of enzymes act to introduce reactive and polar groups into their substrates. Phase I reactions may occur by oxidation, reduction, hydrolysis, cyclization and decyclization, carried out by mixed function oxidases, often in the liver. If the metabolites of phase I reactions are sufficiently