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Essential oils of culinary herbs and spices display agonist and antagonist activities at human aryl hydrocarbon receptor AhR

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ABSTRACT

Essential oils (EOs) of culinary herbs and spices are used to flavor, color and preserve foods and drinks. Dietary intake of EOs is significant, deserving an attention of toxicologists. We examined the effects of 31 EOs of culinary herbs and spices on the transcriptional activity of human aryl hydrocarbon receptor (AhR), which is a pivotal xenobiotic sensor, having also multiple roles in human physiology. Tested EOs were sorted out into AhR-inactive ones (14 EOs) and AhR-active ones, including full agonists (cumin, jasmine, vanilla, bay leaf), partial agonists (cloves, dill, thyme, nutmeg, oregano) and antagonists (tarragon, caraway, turmeric, lovage, fennel, spearmint, star anise, anise). Major constituents (> 10%) of AhR-active EOs were studied in more detail. We identified AhR partial agonists (carvacrol, ligustilide, eugenol, eugenyl acetate, thymol, *ar*-turmerone) and antagonists (*trans*-anethole, butylidine phtalide, R/S-carvones, *p*-cymene), which account for AhR-mediated activities of EOs of fennel, anise, star anise, caraway, spearmint, tarragon, cloves, dill, turmeric, lovage, thyme and oregano. We also show that AhR-mediated effects of some individual constituents of EOs differ from those manifested in mixtures. In conclusion, EOs of culinary herbs and spices are agonists and antagonists of human AhR, implying a potential for food-drug interactions and interference with endocrine pathways.

1. Introduction

Essential oils (EOs), also known as ethereal oils, volatile oils or oils of plant, are natural plant products exhibiting various biological activities. They are concentrated hydrophobic liquids (containing mainly terpenes, ethers, esters, alcohols, aldehydes, hydrocarbons, carboxylic acids etc.) that are obtained by distillation, steam distillation, expression, cold pressing, resin tapping and solvent extraction from plant materials (Tongnuanchan and Benjakul, 2014). The first mention about turpentine oil is ascribed to Greek physician and botanist Pedanius Dioscorides (40–90 A.D.), in his book *De Materia Medica*. The first systematic investigation of essential oils is attributed to M.J. Dumas, who published his results in 1833. Currently, EOs are used mainly in cosmetics (perfumes, soaps, house hold cleaning), food industry and gastronomy (flavoring foods and drinks) and for medicinal applications (aromatherapy, baths, antiseptics, carminatives, diuretics etc.). A discrete group of EOs comprises those obtained from culinary herbs and spices, which are used particularly to flavor, color and preserve foods and drinks. There is an increasing consumption of EOs of culinary herbs and spices in gastronomy, when a number of cookery books and recipes are available. Thereby, dietary intake of essential oils and their constituents is significant, deserving an attention in terms of pharmacology, endocrinology and toxicology.

The aryl hydrocarbon receptor (AhR) is a ligand-activated transcription factor belonging to the family of basic helix-loop-helix transcription factors. It is transcriptionally active in the form of heterodimer with AhR nuclear translocator (ARNT), which binds to xenobiotic responsive element XRE (Denison et al., 2002). A typical target gene for AhR is cytochrome P450 isoform CYP1A1, which is involved in the metabolism of xenobiotics (e.g. polyaromatic hydrocarbons) and endogenous compounds (e.g. eicosanoids). This enzyme is also involved in the process of chemically-induced toxicity and carcinogenesis, because it causes production of free radicals and it converts pro-carcinogens to ultimate carcinogens (Go et al., 2015; Stejskalova and Pavek, 2011). AhR is involved in many cellular and biological processes, including regulation of the cell cycle, DNA repair, immune response, apoptosis, xeno-protection etc. The activators and ligands of AhR comprise diverse exogenous and endogenous compounds (Denison and Nagy, 2003; Stejskalova et al., 2011). The activation of AhR by xenobiotics was linked to various toxicities and pathologies in humans, including skin toxicity (induction of chloracne) (Forrester et al., 2014; Fabbrocini et al., 2015), liver fibrosis (Pierre et al., 2014), atherosclerosis (Wu

Abbreviations: AhR, Aryl Hydrocarbon Receptor; ARNT, AhR Nuclear Translocator; EO, Essential Oil

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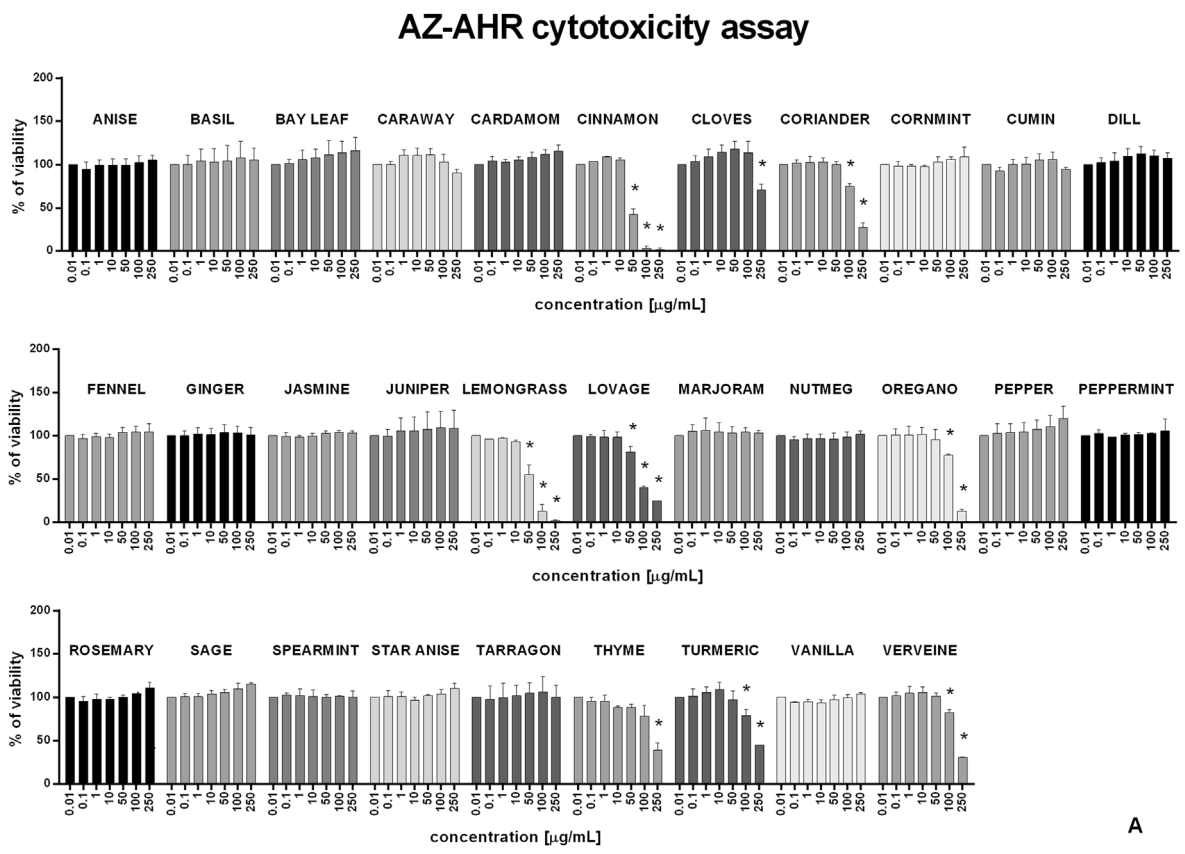

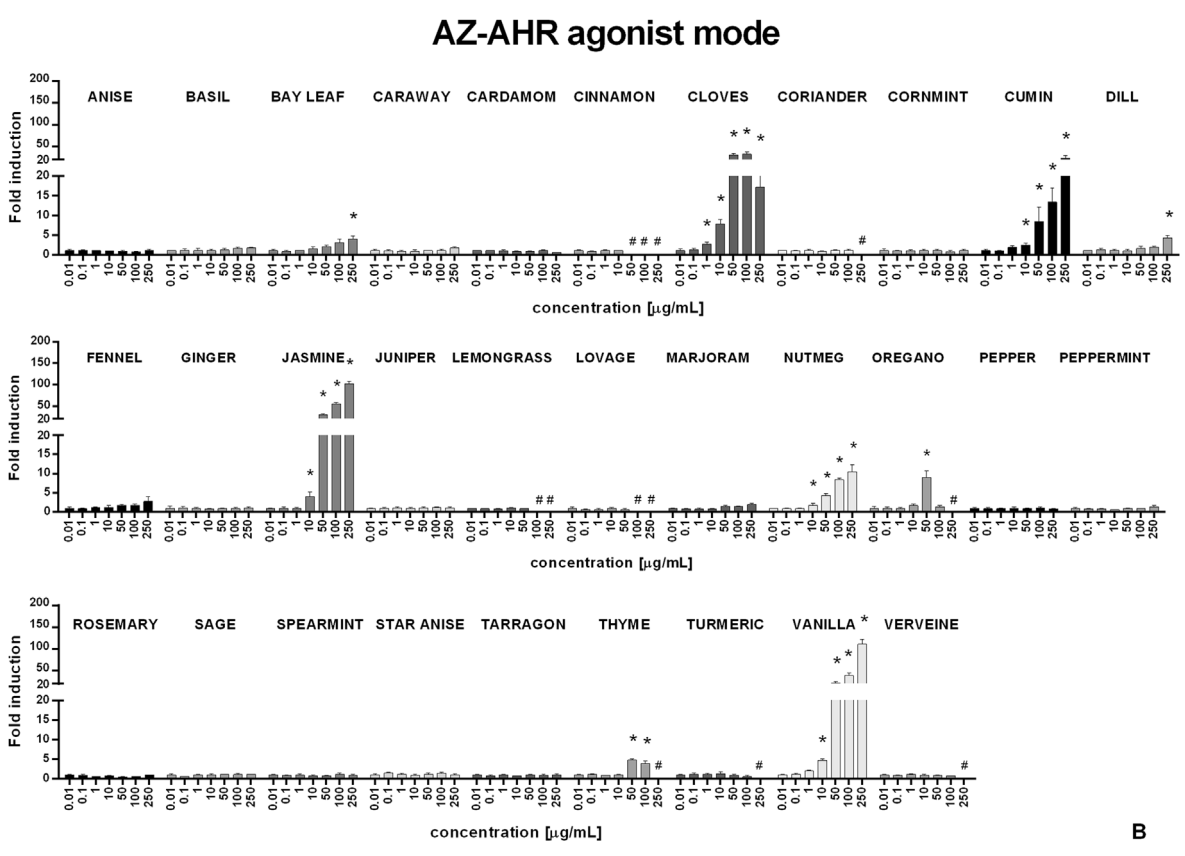

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