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An update on alkylresorcinols – Occurrence, bioavailability, bioactivity and utility as biomarkers

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ABSTRACT

Alkylresorcinols (AR) with alkyl chains in the range of C15 to C25 are phenolic lipids particularly abundant in the outer parts of wheat and rye kernels and in food products containing these parts. The content in whole grain and bran products is high (200–4000 μg/g), whereas only trace-levels are detected in refined products. Alkylresorcinols are absorbed in humans in proportion to intake and have therefore been suggested and evaluated as biomarkers for whole grain wheat and rye intake. In humans, plasma AR concentrations reach micromolar concentrations immediately after whole grain wheat and rye product consumption and nano-molar levels at fasting conditions. Results from different model studies have indicated that AR may have some bioactivities including enzyme inhibition, suppression of adipocyte lipolysis and inhibition of colon cancer tumor growth but it is currently unknown whether AR bioactive *in vivo* or not. This chapter details the recent research findings on alkylresorcinols with emphasis on their occurrence, bioavailability, bioactivity and utility as biomarkers.

1. Introduction

Alkylresorcinols, 1,3-dihydroxy-5-n-alkylbenzenes (AR), are phenolic lipids present in several plant families and in some algae, mosses, fungi, bacteria, and marine sponges (Kozubek & Tyman, 1999). Among commonly consumed foods, AR are mainly found in the outer parts of wheat and rye grains, where homologues with alkyl chains in the range C15–C25 dominate, although derivatives with unsaturated and oxygenated side chains also exist (Fig. 1). The dietary intake of AR is high, particularly in the Scandinavian countries, Germany, Poland, and the Baltic States, where wholegrain rye bread is a commonly consumed traditional food. In Sweden and the UK, AR intake is about 18 and 12 mg/day, respectively (Ross, Becker, Chen, Kamal-Eldin, & Åman, 2005). AR are absorbed by humans and can be detected in blood plasma, erythrocytes, adipose tissue, and in the form of polar metabolites in urine (Jansson et al., 2010; Landberg et al., 2006; Landberg, Åman, Adlercreutz, Vessby, & Kamal-Eldin, 2009a; Linko & Adlercreutz, 2005; Nagy, Ross, Fay, Bourgeois, & Kussmann, 2008; Ross et al., 2003a; Ross, Åman, & Kamal-Eldin, 2004a). Thus, dietary AR are bioavailable in the human body and may have certain bioactivities *in vivo* (Ross, Kamal-Eldin, & Åman, 2004b). In addition, AR have been found to reflect

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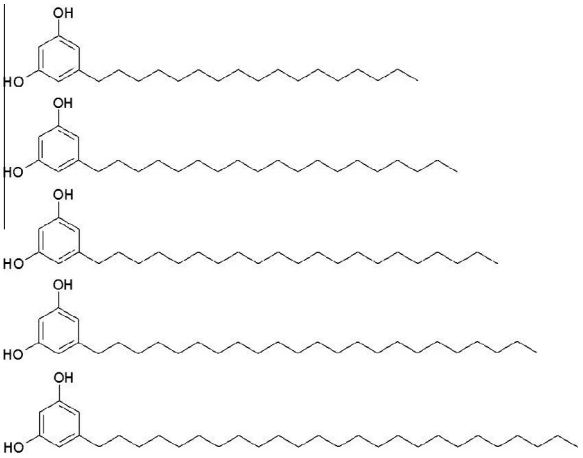

Fig. 1 – The major 5-n-alkylresorcinols in cereal grains, with odd numbered alkyl chains in the range C17:0–C25:0 (from top to bottom).

whole grain and bran intake of wheat and rye, and are currently used as objective biomarkers of these cereals in observational and intervention studies (Landberg et al., 2012; Landberg, Åman, Hallmans, & Johansson, 2013; Ross, 2012). This paper contribution current knowledge on cereal alkylresorcinols with the emphasis on their absorption, distribution, metabolism, and excretion, as well as their bioavailability, potential bioactivities, and utility as biomarkers of whole grain wheat and rye intake.

2. Alkylresorcinol in grains and foods

Alkylresorcinols are located in the outer cuticula of the testa/inner cuticula of the pericarp in barley, wheat, and rye grains, although barley contains only small amounts in comparison with wheat and rye (Fig. 2) (Landberg, Kamal-Eldin, Salmenkallio-Martilla, Rouau, & Åman, 2008a). Due to their presence in these outer parts of the kernel, they are found in high amounts only in whole grain and bran products of these cereals, and in low amounts in refined flour or products (Mattila, Pihlava, & Hellström, 2005; Ross & Kochhar, 2009). In whole grain rye, the AR content is about 268–1444 μg/g dry matter (DM), while that in bran and refined flour is 2400–4100 μg/g DM and 40–280 μg/g DM, respectively. In whole grain wheat, the content is typically in the range 220–943 μg/g DM, while that in refined flour is up to 50 μg/g DM (Andersson, Kamal-Eldin, Fraś, Boros, & Åman, 2008a; Chen, Ross, Åman, & Kamal-Eldin, 2004; Kulawinek, Jaromin, Kozubek, & Zarnowski, 2008; Mattila et al., 2005; Nyström et al., 2008; Ross, Kamal-Eldin, Jung, Shepherd, & Åman, 2001; Ross & Kochhar, 2009; Ross et al., 2003b). In cereal-based foods, the AR content and relative homologue composition vary considerably in different whole grain wheat and rye products, e.g. crisp bread (490–1007 μg/g DM), rye soft bread (197–686 μg/g DM), pasta with rye bran (262–402 μg/g DM), muesli (124–143 μg/g DM), wheat bran breakfast cereals (1784 μg/g DM) whole meal wheat bread (142–353 μg/g DM), wheat crisp bread (58–420 μg/g DM) and wheat biscuits (57 μg/g DM) (Chen et al., 2004; Menzel et al., 2012; Ross et al., 2003b).

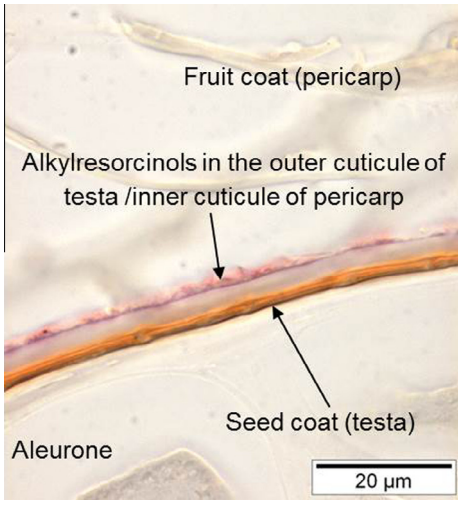

Fig. 2 – Light microscopy of a transverse cryo-section of a rye grain kernel stained by Fast Blue B. Alkylresorcinols appear violet in a specific layer between the seed coat (testa) and fruit coat (pericarp). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

The total AR content typically varies substantially within and between species, but the relative homologue distribution is rather constant within species, with a C17:0/C21:0 ratio of ~1 for rye, ~0.1 for common and spelt wheat, and ~0.01 for durum wheat (Chen et al., 2004; Landberg, Kamal-Eldin, Andersson, & Åman, 2005; Ross et al., 2003b). The AR content in cereals is a highly heritable phytochemical component, but it is also affected by environmental factors such as soil composition, fertilization, and treatment with pesticides (Andersson, Kamal-Eldin, & Åman, 2010a; Shewry et al., 2010).

In foods, AR form starch-lipid complexes, which must be broken down to allow accurate quantification. A hot 1-propanol extraction method (Morrison, Milligan, & Azudin, 1984), designed to completely extract lipids from starch-lipid complexes, can be used for this purpose. Accelerated solvent extraction can also be used, with similar results to the hot 1-propanol method obtained in a much shorter time (Holt, Moreau, DerMarderosian, McKeown, & Jaques, 2012). The AR content remains stable in the matrix throughout food processing, as shown by the good correlation between measured content in ingredients and in final products reported in two separate studies (R^2 = 0.91 and 0.83, respectively) (Andersson, Åman, Wandel, & Frølich, 2010b; Chen et al., 2004). The AR content has therefore been suggested for use as a marker for the whole grain wheat and rye content of cereal food products (Andersson et al., 2010b; Chen et al., 2004; Ross et al., 2003b). Since the AR homologue composition is rather stable within cereal species, the C17:0/C21:0 ratio can be used to determine whether a product is made of rye or wheat, or whether it is a mixture of the two (See Fig. 3).

3. Alkylresorcinol pharmacokinetics

The extent and rate of absorption, distribution, metabolism, and excretion (ADME) and related parameters have been