

Polyphenol Ingredients and Health Effects of Green Oats: A Brief Update

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ABSTRACT

Green oat, also known as wild green oat, is a principal cultivated species harvested at their prime development stage, when still green and packed full of active functional nutrients, contributing to attenuating oxidative damage, reducing inflammatory reaction, hindering tumor progression and promoting cognitive health. The biological and physiological effects, to a large extent, are attributed to a variety of bioactive phytochemicals, encompassing β -glucan, dietary fiber as well as phenolic compounds, particularly Avenanthramides, the exclusive phenolic compounds in oats, demonstrating multiple and remarkable biological activities such as antioxidation, anti-inflammation, antineoplastic and immunomodulatory effects. In consideration of the promising edible and medicinal values, hence, this article will illustrate the underlying values in food and health of green oat, or its extracts, from the amounts and composition, biological effects concerned as well as the possible molecular mechanisms involved.

1. Introduction

Green oat (*Avena sativa* L.), also known as Wild Green Oat, belongs to *Avena* L., which includes 29 to 31 species, depended on the classification scheme, of wild and domesticated annual grasses in the family Gramineae (Poaceae)(Leggett, 1992). As for classification, the genus of green oat is *Avena* L., and this gramineous plant belongs to Liliidae, a subclass of monocots. And the primary species cultivated throughout the world, typically Occident, is *Avena sativa*. As one type of oat, the fifth most economically important cereal worldwide, green oat is cultivated in temperate regions worldwide, especially those of North America and Europe(Peterson & Murphy, 2000). Green oat is originated in Switzerland and has been recorded in the German pharmacopoeia for more than 200 years. As an annual crop, oat has been reported to be cultivated for more than 2000 years(Sang & Chu, 2017), and consumed in China, the USA, Switzerland, Denmark, Finland, Norway and Sweden. In addition to the edible application as cereal, green oat, or its extracts exactly, has a long history of medicinal use in antianxiety and skincare(Abascal & Yarnell, 2004; Reynertson et al., 2015). Furthermore, it is noteworthy that the bioactive phytochemicals in oat extracts, typically Avenanthramides, have been shown to have a favorable effect on antioxidation, reducing inflammatory reaction, hindering tumor progression, improving hyperlipidemia as well as promoting cognitive health, about which a large range of people are concerned, consequently, an increasing amount of attention is paid to green oat or its products derived, which is mostly due to the bioactive compounds in oat, esto a variety of bioactive phytochemicals, encompassing β -glucan, dietary fiber as well as phenolic compounds, particularly polyphenols as well as oat exclusive Avenanthramides.

2. Composition and effects of the polyphenol compounds in green oat

As a typical subvariety of whole grains, oat is, in addition to carbohydrates, rich in protein, lipids, dietary fiber, vitamins, minerals, and other bioactive substances, which intensify health benefits by reducing the risk of a number of clinical syndromes of great concern, such as hyperlipidemia, cardiovascular diseases and cancers. Of the bioactive ingredients in oat, polyphenols and their derivatives are various and abundant.

2.1 Phenolic compounds

Phenolic compounds are one of the largest chemical class of the secondary metabolites synthesized by plants. As for the structural feature, phenolic compounds, ranging from simple phenols to polymerized compounds, contains benzene rings, with one or more hydroxyl substituents. Phenolic compounds in oat comprise phenolic acids, flavonoids and others, such as stilbenes, lignans (Fig.1). As for the major phenolic compounds in the oat grain, phenolic acids, free, conjugated or bound, consist of hydroxybenzoic acid, including protocatechuic, vanillic, *p*-hydroxybenzoic, gallic and syringic acids, and hydroxycinnamic acid, encompassing ferulic, *p*-coumaric, *o*-coumaric, caffeic and sinapic acids(Li, Shewry, & Ward, 2008). Oat products are regarded as an abundant supply of polyphenols, which contain a considerable amount of phenolic acids, ranging from 15.79 and 25.05 mg, (9.9–19.33 mg bound, 4.96–5.72 mg free and conjugated) in oat products, including oat bran concentrate, oat bran, flaked oats, rolled oats and oatcakes(Soycan et al., 2019). As for the constituents with biological and physiological effects in the oat grain, ferulic acid, the major phenolic acids in oat products, exerts an anti-tumor activity by targeting fibroblast growth factor receptor 1(FGFR1)-mediated angiogenesis(G. W. Yang, Jiang, & Lu, 2015). And *p*-Coumaric acid(trans-4-Hydroxycinnamic acid), an isomer of cinnamic acid with oral activity, has antibacterial, anti-inflammatory and antioxidant activities as well as anti-tumor effects, via promoting apoptosis and inhibiting cell

proliferation(Hu et al., 2020) (Lou et al., 2012; Rafiee, Moaiedi, Gorji, & Mansouri, 2020; Sharma, Chellappan, Chinnaswamy, & Nagarajan, 2017). Similarly, gallic acid (3,4,5-Trihydroxybenzoic acid) has resemble biological activities and effects, which is an free radical scavenger to inhibit cyclooxygenase-2 (COX-2)(Amaravani, Prasad, & Ramakrishna, 2012).

2.2 Avenanthramides

In particular, Avenanthramides (AVAs), present exclusively in oats or its products, are the most abundant phenolic alkaloids and have prominent physiological effects. In the chemical structure, avenanthramides are based on an amide conjugate of anthralinic acid and hydroxycinnamic acids, and the 3 major types in oat are 2p (Avenanthramide A), 2f (Avenanthramide B), and 2c (Avenanthramide C), correspondingly with p-coumaric, and ferulic, and caffeic acids (Fig.2), in which Avenanthramide 2c has the highest total antioxidant capacity(J. Yang, Ou, Wise, & Chu, 2014). As for the distribution of oat, AVAs are generally present in all milling fractions and commercial oat products, which are more abundant in oat bran (1.3–12.5 mg/100 g) than other tissues, including oat germs, leaves and roots, while more deficient in the grains (42.07 mg/100 g)(Xie et al., 2024). Furthermore, the comparison of different parts of the grains was made in this review, which is based on the AVA content from five oat samples, and illustrates the fact that levels of AVAs (2p, 2f, 2c) are significantly higher in groats than those in oat hulls. Meanwhile, from another perspective, it is not difficult to find the fact that the amount of the specific AVA is not correlated with its antioxidant activity, as AVA 2c is not the most abundant while it is considered to have the highest antioxidant capacity (Fig.3)(Bratt et al., 2003). Besides, AVAs vary in different, species, growth stages, growth conditions, and locations(Xie et al., 2024).

When it comes to the biological and physiological effects, the remarkable and excellent antioxidant activity of oat extracts have to be mentioned. Taking the 3 major types of AVAs as an instance, AVA A, B and C have been shown to be

associated with the fresh taste and nutritional value of the oat products and to be heat stable, thus, to a large extent, they protect oat as antioxidants against rancidification, especially autoxidation of polyunsaturated fatty acids (Molteberg, Solheim, Dimberg, & Frølich, 1996). Notably, AVAs have been demonstrated a variety of biological effects in human cells, in which antioxidation, anti-inflammation as well as antineoplastic activity are of great concern (Xue, Teng, Chen, Li, & Wang, 2021).

3. Effects and mechanisms of AVAs of concern

3.1 Antioxidation

Oat has been regarded as an excellent food source for antioxidants for a long time (Peters, 1937). In terms of the functional composition, AVAs, oat specific phenolic alkaloid, generally, exhibit potent antioxidant properties both *in vitro* and *in vivo*, even clinical trials are included. As for the antioxidant mechanisms, antioxidant enzymes, such as superoxide dismutase enzymes (SODs), glutathione peroxidases (GPx) and catalase (CAT), are considered to be predominant in the effectiveness of antioxidant defense in the body. SODs are recognized to be an important antioxidant defense against reactive oxygen species (ROS)-mediated injuries, such as aging and chronic inflammation. And GPx is a family of antioxidant enzymes vital for maintaining ROS homeostasis, promoting hydrogen peroxide metabolism and protecting cell membrane from oxidative damage. In most cases, AVAs enhance the antioxidant capacity by means of upregulating the activity or the expression of antioxidant enzymes, consequently defend against ROS-mediated injuries (Fig. 4) (Liu et al., 2011). According to a clinical study, the plasma concentration of reduced glutathione, an eminent antioxidant in the body, markedly increased when subjects consumed AVA-enriched oat extracts. To be specific, reduced glutathione in plasma was elevated by 21% at 15 min and by 14% at 10 h after consumption of 1 g AVA-enriched mixture (Chen, Milbury, Collins, & Blumberg, 2007). In particular, AVA 2c could reduce H₂O₂-induced oxidative stress in normal

human dermal fibroblasts by regulating the level and the activity of antioxidant enzymes, including, SOD1, GPX1, heme oxygenase 1 (HMOX1) and CAT(Wang & Eskiw, 2019). Moreover, AVA-rich oat extracts possess effective antioxidant activity against D-galactose-induced oxidative stress, by elevating the activity of the antioxidant enzymes, such as SOD and GPx, as well as upregulating their gene expression(Ren, Yang, Niu, Liu, & Ren, 2011).

3.2 Anti-inflammation

It has been established that AVAs have anti-inflammatory properties both in histocytes(Kang et al., 2018) and immune cells(Dhakal et al., 2019), involved in dozens of diseases especially hypersensitivity (Sur, Nigam, Grote, Liebel, & Southall, 2008) and neurodegenerative diseases (NDDs) (Wankhede et al., 2023). Nuclear factor- κ B (NF- κ B) signaling has been regarded as a pivotal pathway in inflammatory and immune responses via regulating a large array of genes involved. RelA and p50 heterodimers, generally sequestered in the cytoplasm by the inhibitory I κ B (inhibitor of NF- κ B), the downstream substrate of phosphorylation-dependent activation of the IKKs (I κ B kinases), are responsible for transcription of target genes when the canonical NF- κ B pathway is activated, while with NF- κ B heterodimers formed by RelB and p52 (p100 as the precursor) activating downstream pathways in non-canonical NF- κ B pathway(Yu, Lin, Zhang, Zhang, & Hu, 2020). In the canonical NF- κ B pathway, the inhibitory proteins are phosphorylated and subjected to the ubiquitination-dependent degradation by proteasome, liberating the NF- κ B, translocating to nucleus and subsequently transcriptionally activating the target genes(Yu et al., 2020). Exactly, AVAs have potent inhibitory effects on NF κ B-mediated inflammatory responses mostly via attenuating IKK β phosphorylation, consequently downregulating the expression of proinflammatory cytokines (Fig. 5)(Guo, Wise, Collins, & Meydani, 2008; Kang et al., 2018). AVAs has been shown an inhibitory activity of downregulating I κ B in keratinocytes with decreased phosphorylation of RelA of the incipient NF- κ B,

and a reporting system confirmed the fact that cells treated with AVAs performed a significant inhibition of tumor necrosis factor-alpha (TNF-alpha) induced NF-kappaB luciferase activity subsequently with reduced release of interleukin-8, and the anti-inflammatory effects that AVAs induced generally are involved in the transcriptional activation level, in particular the expression of genes encoding pro-inflammatory cytokines(Sur et al., 2008; Wang & Eskiw, 2019). Besides, AVA 2c was shown to inhibit the expression of a NF-kappaB-dependent reporter gene activated by TNFR-associated factor 2 and 6 and NFkB-inducing kinase, which is involved in non-canonical NF-kB pathway(Guo et al., 2008). In addition, it is likely that AVAs are potential modulators of the PI3K (Phosphoinositide 3-kinase) signaling pathway, which is implicated in the pathogenesis of various NDDs including Parkinson's disease and Alzheimer's disease. Specifically, AVA 2c modulates the S9-GSKβ of the PI3K/AKT pathway with altered amyloid-β aggregates in Alzheimer's disease(Wankhede et al., 2023).

3.3 Antineoplastic activity

Nowadays an increasing number of people, both teenagers and the elderly, suffer from cancers. It was noteworthy that AVAs have antineoplastic activity. Specifically, AVAs have antiproliferative, apoptosis-promoting, anti-inflammatory, pro-senescent and latent antimetastatic properties in tumorigenesis and tumor development (Fig. 6). For instance, AVAs could inhibit the proliferation of colorectal adenocarcinoma cells and hepatoma cells, via activating caspases 9, 8, and 3, which are major executors in cell apoptosis []. And AVAs perform negative regulation on a number of genes conducive to survival or angiogenesis, such as BIRC5 (Baculoviral inhibitor of apoptosis repeat-containing 5), HIF1A (hypoxia-inducible factor-1 alpha), and VEGFA (Vascular endothelial growth factor A)(Scarpa, Antonini, Palma, Mari, & Ninfali, 2018). Furthermore, AVAs-enriched extracts of oats have been demonstrated the capacity of inhibiting COX-2/ PGE2 (Prostaglandin E2) in

lipopolysaccharide-stimulated mouse peritoneal macrophages, which are pivotal in mediating inflammatory microenvironment and angiogenesis in cancer cells(Guo et al., 2010; Hashemi Goradel, Najafi, Salehi, Farhood, & Mortezaee, 2019). Moreover, a recent study reveal that AVA 2c exerts pro-senescence by attenuating β -catenin-mediated transactivation of miR-183/96/182 cluster, subsequently upregulating p21 and p16. In addition, senescence promoting effects induced by AVA 2c is also involved in facilitating p53-mediated p21 transactivation via suppressing β -catenin in colorectal cancer cells(Fu et al., 2022). As for potential applications of AVAs, yeast avenanthramides, synthetic compounds with a structural similarity to bioactive oat avenanthramides, are effective in inhibiting the migration of cancer cells as well as epithelial-mesenchymal transition, which is pivotal in the initiation of tumor metastasis(Finetti et al., 2018).

4. Perspectives of oat derived products

Oat is one of the most promising cereal grains for product development both for edible and medicinal use. And Green oat is full of bioactive nutrients, contributing to attenuating oxidative damage, reducing inflammatory reaction, hindering tumor progression and promoting cognitive health. Structurally, bioactive substances, typically polyphenols and the exclusive AVAs, are abundant and heat-stable in oat. As for physiological and biological effects, oat extracts have been shown remarkable and multiple biological activities, such as antioxidant, anti-inflammatory and antineoplastic properties, which is of great concern both in the elderly as well as teenagers in recent years. Besides, oat is a preferred source for chronic disease prevention. A study reveals that long-term AVA supplementation benefits human health, with the descending generation of ROS as well as the dropping inflammatory factors after an acute bout of eccentric exercise(Koenig et al., 2016). Noteworthily, it is the fact that green oat preparations have been used to promote human health in long-term treatment, with improving the symptoms of acute and chronic anxiety and

tension, neurasthenia as well as cardiovascular disease, while enhancing the physical performance and energy levels, which are suitable for a variety of people, especially in sub-health status, regardless of gender and age, indicating a broader range of consumers or customers in oat derived products.

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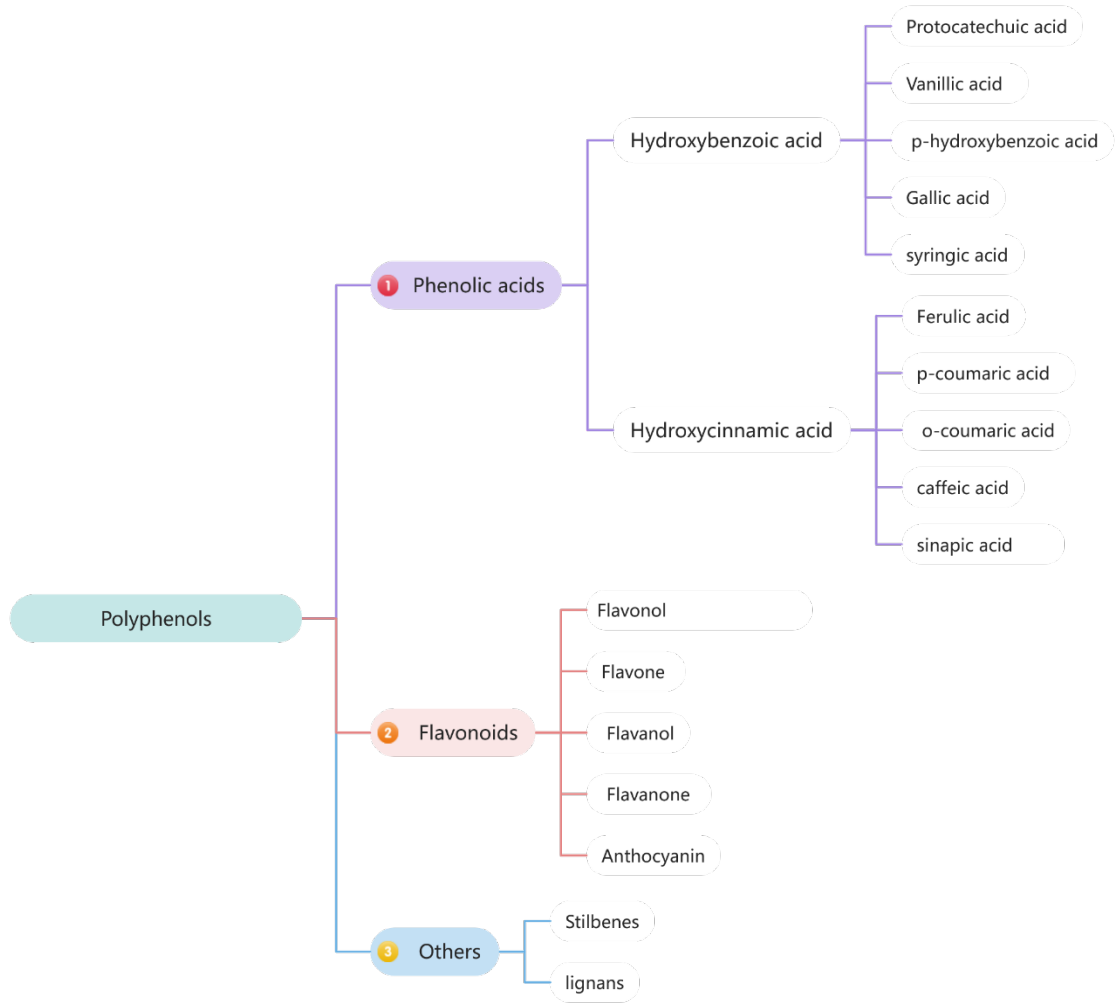


Fig.1 Composition and classification of polyphenols in Oat

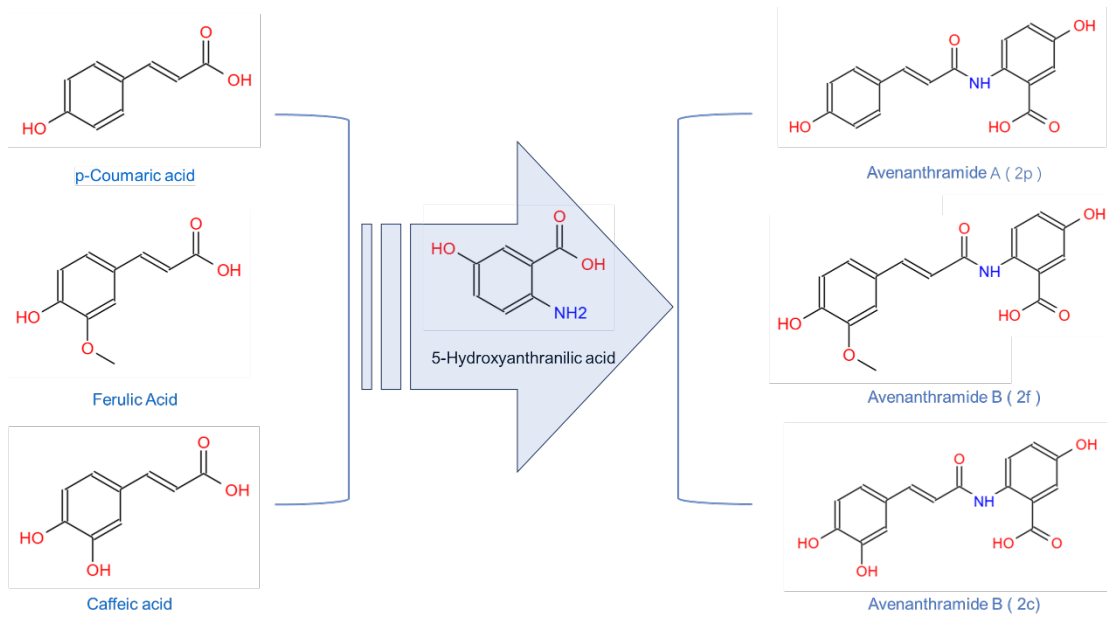


Fig.2 Molecular structure of the primary components of Avenanthramides.

Levels of AVAs in Groats and Hulls of Oats

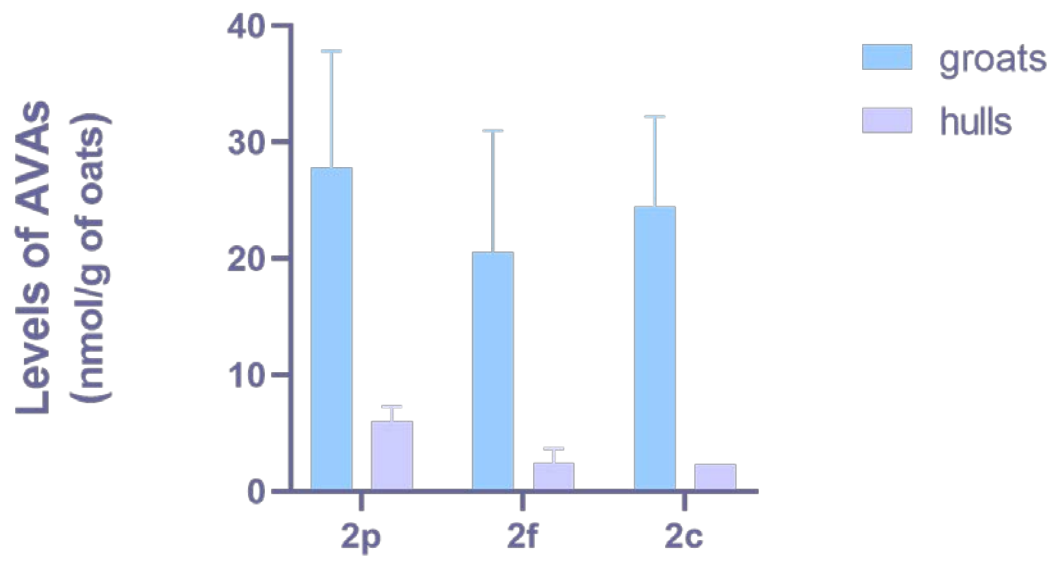


Fig.3 Levels of AVAs in groats and hulls of oats

Fig.4 Possible mechanism of the antioxidant effects of Avenanthramides

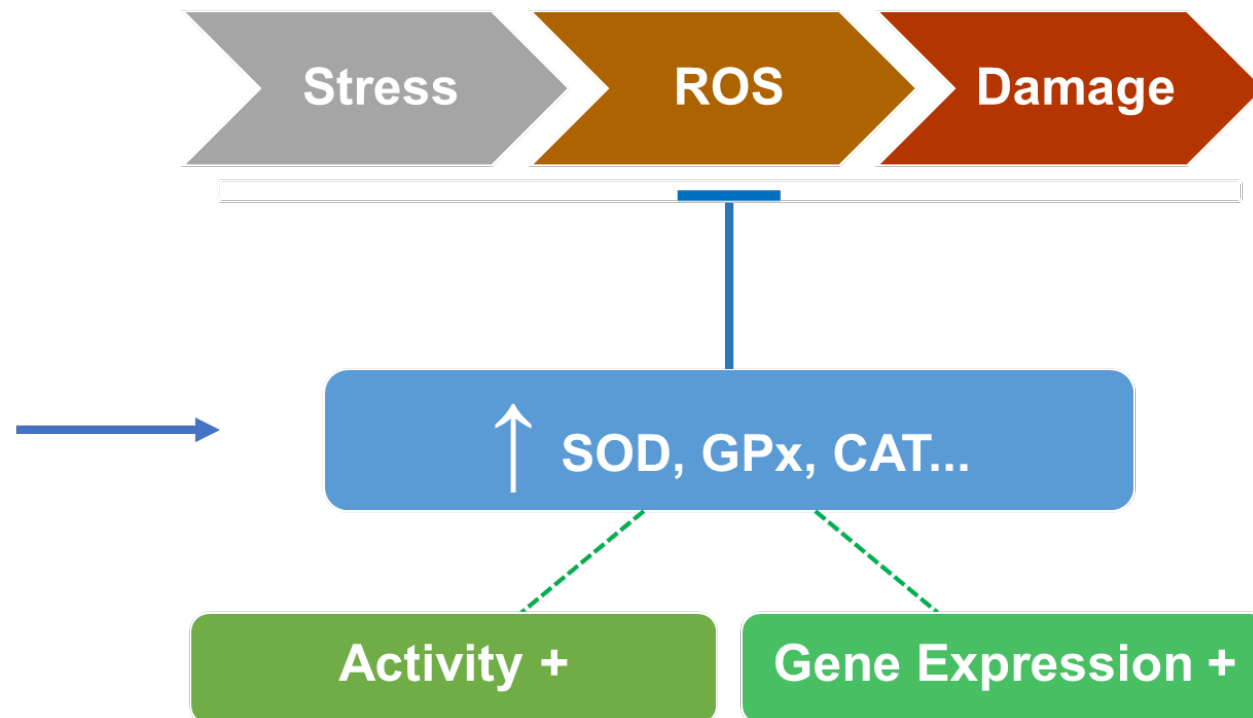
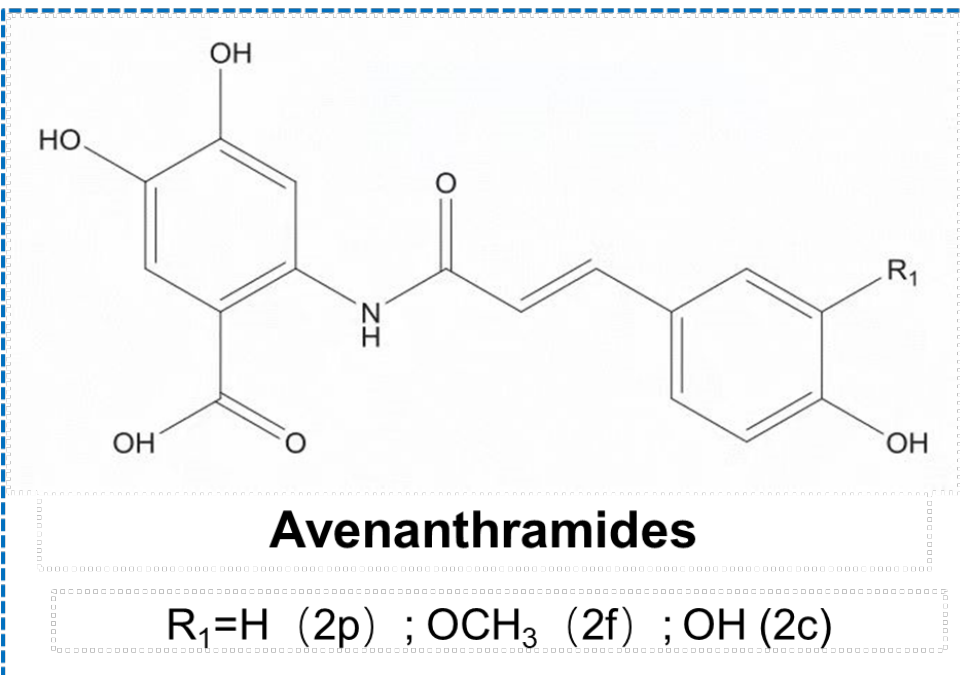


Fig.5 Possible mechanism of the anti-inflammatory effects of Avenanthramides

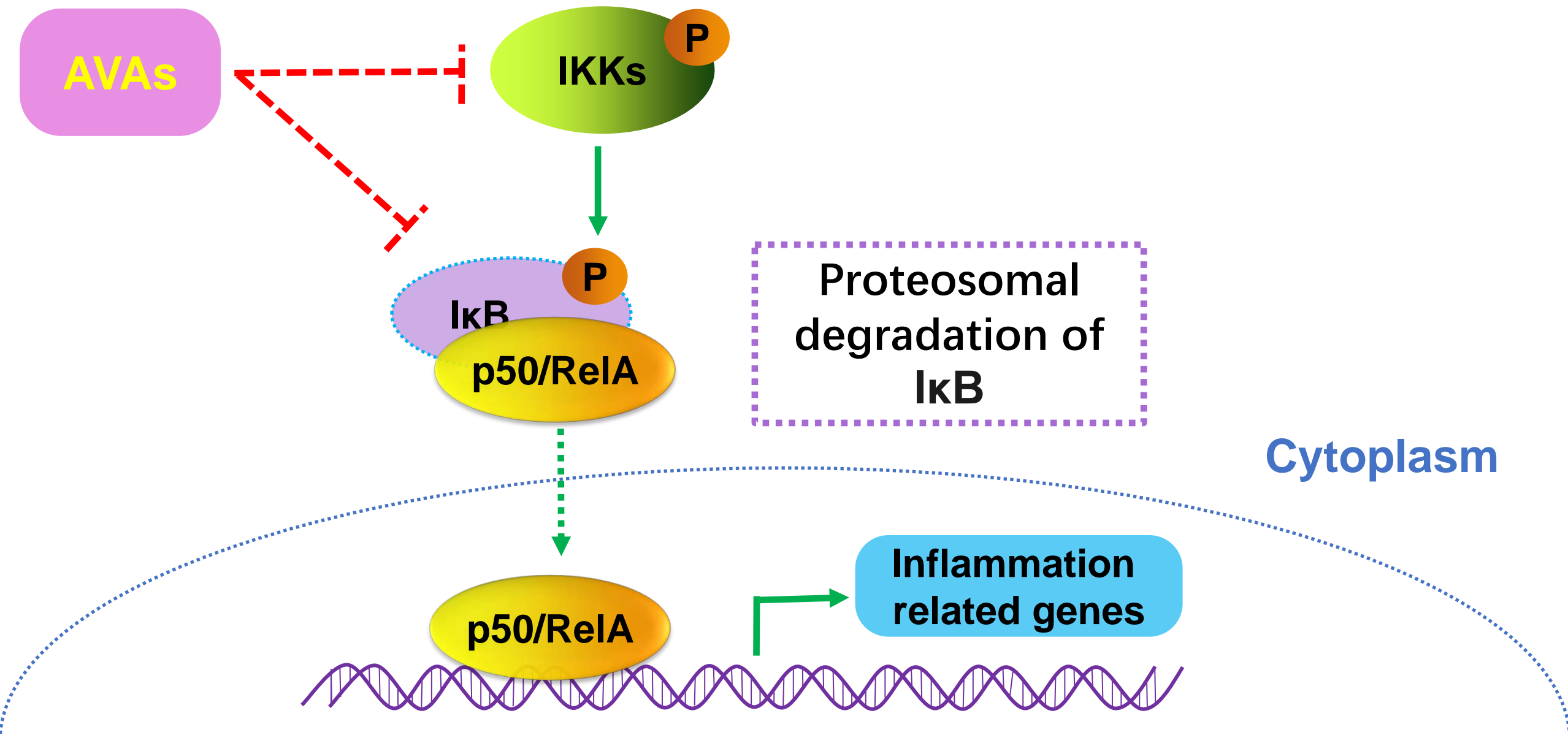


Fig.6 Possible mechanism of the antineoplastic activity of Avenanthramides

