Medicinal plant polyphenols in vitro activity on glycation and oxidative stress related to vascular diseases

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BACKGROUND and AIM

Evidences indicate that oxidative stress and glycation play a crucial role in aging, neurodegenerative and cardiovascular diseases. Oxidative stress is linked with reactive oxygen species (ROS), whose harmful effects can lead to several pathological conditions like vascular alterations, diabetes complications and inflammation. Moreover, ROS and oxidative stress can directly contribute to glycation reactions because of the formation of reactive α-oxoaldehydes and advanced glycation end-products (AGEs). The glycation process is characterized by a non-enzymatic reaction between aldehyde or keto groups in sugars and free amino-residues in proteins, which lead to the formation of AGEs. Glycation and AGEs cause the irreversible modification of the proteins structure and the consequent loss of their functionality, causing detrimental effect in vasculature. Thus, compounds which counteract oxidative stress and glycation may assume an important role in the prevention of vascular damage.

MEDICINAL PLANT POLYPHENOLS

Natural phenolic compounds and flavonoids have received attention for their biological effects, such as antioxidant and antiglycative activities. The polyphenols studied in this research are characteristic phytoconstituents of several medicinal plants widely used in traditional medicine such as: baicalein (from Scutellaria baicalensis G.), eupatorin (Eupatorium semiserratum DC.), galangin (Alpinia officinarum L.), magnolol (Magnolia officinalis L.), myricetin (Myrica rubra S. Z.), oleuropein (Olea europaea L.) and silybin (Silybum marianum L.).

GLYCATION

The in vitro antiglycative activity of the polyphenols was evaluated using the BSA assay: AGEs were determined using bovine serum albumin (BSA) as protein substrate and glucose, ribose or glyoxal as glicative agents. The AGEs formation was experimentally measured using fluorimetry, setting $\lambda_{ex}$ at 355 nm and $\lambda_{em}$ at 460 nm. The polyphenols concentrations used were 5-10-50 μM.

Antioxidant activity

In the experimental model involving HUVEC cells, the aim was to evaluate the potential role of several compounds related to hyperglycemia and glycation, such as glycated albumin, glyoxal and glucose, to induce oxidative stress (on the left). The figures below show the antioxidant activity of the selected natural compounds (1-5 μM) against the oxidative stress induced by high glucose (25 mM), assessed using the DCDH-DA assay.

RESULTS and CONCLUSION

The results of AGEs determination showed that most of the polyphenols at the higher concentration displayed antiglycative activity in all experimental conditions. In the BSA-glucose assay, only baicalein exerted the antiglycative activity at 5 μM. In the BSA-ribose assay, the highest antiglycative activity was seen for baicalein, eupatorin and galangin; then, magnolol and eupatorin were able to significantly inhibit the AGEs formation induced by glyoxal. The results from ROS detection assay showed that the glycation products known as glycated albumin and glyoxal were not able to directly induce oxidative stress in HUVEC in the assay conditions, however high glucose induce ROS formation in HUVEC after 24 h treatment. In basal condition, baicalein and galangin at 1-5 μM significantly reduced the ROS formation, whereas all the polyphenols, but especially baicalein and galangin, reduced the ROS formation induced by high glucose and displayed antioxidant activity. All together, the results obtained motivate further researches on the activities of polyphenols against oxidative and glycative damages in order to understand their potential role in the prevention of vascular diseases.

Fig. 1. Chemical structure of the plant-derived polyphenols.

Fig. 2. Antiglycative activity of selected polyphenols expressed as inhibition of AGEs formation induced by glucose, ribose, and glyoxal. Aminoguanidine (AG) was used as positive control. Each value represents mean ± SD of at least three experiments, * p > 0.05 vs. controls (ctrl).

Fig. 3. Oxidative stress in HUVEC. (A) ROS formed after treatment with glycated albumin, glyoxal and high glucose for 24 h. (B) Antioxidant effect of selected polyphenols baicalein, eupatorin and galangin in HUVEC after 2h pre-treatment (basal condition). (C) Antioxidant activity of baicalein, eupatorin and galangin expressed as percentage of ROS formation in HUVEC after 24 h treatment with high glucose.

Each value represents mean ± SD of at least three experiments, * p > 0.05 vs. controls (ctrl).