EFFECTIVE COMPOUNDS OF POMEGRANATE AND THEIR EFFECT ON ANIMAL CELLS

Dagmara Packová*,1, Nora Maruniaková1, Marek Halenár1, Ángel A. Carbonell-Barrachina2, Adriana Kolesárová1

Address(es): Ing. Dagmara Packová, 1Slovak University of Agriculture in Nitra, Faculty of Biotechnology and Food Sciences, Department of Animal Physiology, Tr. A. Hlinka 2, 949 76 Nitra, Slovak Republic.
2University of Miguel Hernández, Department of Agrifood Technology, Carretera de Beniel, Km. 3, 2, 03312 Orihuela (Alicante), Spain.

*Corresponding author: xpackova@uniag.sk

ARTICLE INFO
Received 22. 10. 2013
Revised 28. 11. 2013
Accepted 8. 1. 2014
Published 1. 2. 2014

INTRODUCTION
Pomegranate - characteristic and effect on animal organism
Punica granatum belongs to the Punicaeae family and exists over 1000 cultivars (Levin, 1994). The pomegranate is a symbol of life, longevity, health etc. (Mahdihassan, 1984) and belongs among one of the oldest known edible fruit. It is cultivated in Iran, Afghanistan, India, Mediterranean countries and to some extent in the USA, China, Japan and Russia. Spain is the main European pomegranate producer and its production is mainly located in the province of Alicante (Raisi et al., 2008; Vardin Fenercioglu, 2003; Calín Sánchez et al., 2010). Pomegranate belongs to fruits, which is very rich on antioxidants (Calín Sánchez et al., 2010) and contains bio-active compounds (Calín Sánchez and Carbonell Barrachina, 2012). For example among protective compounds belong antioxidants - hydroxyalable tannins, that are compound abundant in some fruits and nuts, such as pomegranates, black raspberries, raspberries, strawberries, walnuts, and almonds (Calín Sánchez and Carbonell Barrachina, 2012). Hydroxyalable tannins (antioxidants) are found in aril, rind and capillary membranes. Rinds and capillary membranes are richer source of antioxidant than arils. Among to antioxidants belong punicalagin and ellagic acid (Calín Sánchez and Carbonell Barrachina, 2012). Edible part of pomegranate, 50% from total weight are arils and seed, but more than 50% of bioactive compounds (antioxidants) are described in husk or pulp membranes (antocyanidins, flavonoids, ellagitannins or minerals) (Calín Sánchez and Carbonell Barrachina, 2012). Pomegranate arils are composed of 85% water, 10% sugar (glucose, fructose and sucrose), 1.5% organic acid (citric acid, malic acid, fumaric acid etc.) and bioactive compounds - tannins or ellagitannins (punicalagin, punicalin, ellagic acid etc.) and flavonoids (catechin, quercetin etc.) (Calín Sánchez and Carbonell Barrachina, 2012; Larsky and Newman, 2007). Mineral compounds in pomegranate are in particular potassium, nitrogen, phosphorous, magnesium or sodium. Pomegranate contains antioxidants in aril, rind and capillary membranes (Calín Sánchez and Carbonell Barrachina, 2012). Effect of pomegranate could have utilization in different medicine’s ways, for example from India or Guatemala. Dried peels are decocted in water and used for problems - aphthae, diarrhea or ulcers (Lansky and Newman, 2007).

The pomegranate has a broad range of potentially therapeutic uses, including treatment and prevention of cancer, cardiovascular disease, Alzheimer’s disease, inflammatory disease, oral and skin disease, obesity, erectile dysfunction and diarrhea (Calín Sánchez and Carbonell Barrachina, 2012). Fatty acid from pomegranate play important role in prevention of cardiovascular disease. This fatty acid (linoleic, linolenic and arachidonic acids) can reduce HDL - cholesterol levels (Calín Sánchez and Carbonell Barrachina, 2012). Also compounds of pomegranate could stimulate serotonin and estrogen receptors (Tyagi et al., 2012). Extract from pomegranate has relieving effect on women's menopausal symptoms, anxiety disorders, depression or attention deficit disorders. Ellagic acid introduces health benefits against cancer, cardiovascular diseases and other disease. It is possible, that compounds of pomegranates or their metabolites could have impact on different animal cells and regulate their intracellular mechanism.

Keywords: Antioxidant, apoptosis, ellagic acid, pomegranate, punicalagin

ABSTRACT
This review describes possible effects of antioxidant compounds of pomegranate on animal cells. Pomegranate (Punica granatum L.) fruits are widely consumed. Pomegranate is one of the oldest known edible fruit. Spain is main producer in the Europe. Pomegranate contains bioactive polyphenols - punicalagin with molecular weight 1084. Part of punicalagin's molecule is ellagic acid. The both substances generate total antioxidant capacity of pomegranate. Punicalagin compounds present high antioxidant capacity - approximately 50%, ellagic acid as single molecule has 3% of antioxidant capacity. Punicalagin is molecule with high molecular weight and have to be hydrolised. Colonic microorganism metabolise yield of pomegranate (punicalagin or ellagic acid) to urolithin A and is detected in blood, urine or faeces. Extract from pomegranate can show anticarcinogenic effect, induction of cell - cycle arrest, apoptosis and proliferation. Extract from pomegranate has relieving effect on woman's menopausal symptoms, anxiety disorders, depression or attention deficit disorders. Ellagic acid introduces health benefits against cancer, cardiovascular diseases and other disease. It is possible, that compounds of pomegranates or their metabolites could have impact on different animal cells and regulate their intracellular mechanism.

Keywords: Antioxidant, apoptosis, ellagic acid, pomegranate, punicalagin

INTRODUCTION
Pomegranate - characteristic and effect on animal organism
Punica granatum belongs to the Punicaeae family and exists over 1000 cultivars (Levin, 1994). The pomegranate is a symbol of life, longevity, health etc. (Mahdihassan, 1984) and belongs among one of the oldest known edible fruit. It is cultivated in Iran, Afghanistan, India, Mediterranean countries and to some extent in the USA, China, Japan and Russia. Spain is the main European pomegranate producer and its production is mainly located in the province of Alicante (Raisi et al., 2008; Vardin Fenercioglu, 2003; Calín Sánchez et al., 2010). Pomegranate belongs to fruits, which is very rich on antioxidants (Calín Sánchez et al., 2010) and contains bio-active compounds (Calín Sánchez and Carbonell Barrachina, 2012). For example among protective compounds belong antioxidants - hydroxyalable tannins, that are compound abundant in some fruits and nuts, such as pomegranates, black raspberries, raspberries, strawberries, walnuts, and almonds (Calín Sánchez and Carbonell Barrachina, 2012). Hydroxyalable tannins (antioxidants) are found in aril, rind and capillary membranes. Rinds and capillary membranes are richer source of antioxidant than arils. Among to antioxidants belong punicalagin and ellagic acid (Calín Sánchez and Carbonell Barrachina, 2012). Edible part of pomegranate, 50% from total weight are arils and seed, but more than 50% of bioactive compounds (antioxidants) are described in husk or pulp membranes (antocyanidins, flavonoids, ellagitannins or minerals) (Calín Sánchez and Carbonell Barrachina, 2012). Pomegranate arils are composed of 85% water, 10% sugar (glucose, fructose and sucrose), 1.5% organic acid (citric acid, malic acid, fumaric acid etc.) and bioactive compounds - tannins or ellagitannins (punicalagin, punicalin, ellagic acid etc.) and flavonoids (catechin, quercetin etc.) (Calín Sánchez and Carbonell Barrachina, 2012; Larsky and Newman, 2007). Mineral compounds in pomegranate are in particular potassium, nitrogen, phosphorous, magnesium or sodium. Pomegranate contains antioxidants in aril, rind and capillary membranes (Calín Sánchez and Carbonell Barrachina, 2012). Effect of pomegranate could have utilization in different medicine’s ways, for example from India or Guatemala. Dried peels are decocted in water and used for problems - aphthae, diarrhea or ulcers (Lansky and Newman, 2007). The pomegranate has a broad range of potentially therapeutic uses, including treatment and prevention of cancer, cardiovascular disease, Alzheimer’s disease, inflammatory disease, oral and skin disease, obesity, erectile dysfunction and diarrhea (Calín Sánchez and Carbonell Barrachina, 2012). Fatty acid from pomegranate play important role in prevention of cardiovascular disease. This fatty acid (linoleic, linolenic and arachidonic acids) can reduce HDL - cholesterol levels (Calín Sánchez and Carbonell Barrachina, 2012). Also compounds of pomegranate could stimulate serotonin and estrogen receptors (Tyagi et al., 2012). Extract from pomegranate has relieving effect on women's menopausal symptoms, anxiety disorders, depression or attention deficit disorders (Lee, 2013).

Compounds of pomegranate – Punicalagins and Ellagic acid
Pomegranate contains more bioactive compounds, but ellagitanmins like punicalagin and ellagic acid have the main antioxidant effect have (Seeram et al., 2005).

Punicalagins - characteristic, metabolism and effects
Pomegranate husk is rich on the hydroxyalable tannins - mainly punicalagin, pedunculagin, punicalin (Calín Sánchez and Carbonell Barrachina, 2012). Punicalagins have two isomeric forms in pomegranate: α and β. They belong to group of tannins - polyphenolic compounds. Chemical name of punicalcin is 2,3-(S)-hexahydroxydiphenoyl-4,6-(S,S)-gallagyl-D-glucose (Tyagi, 2012). Punicalagin is connected gallic acid with ellagic acid through molecule of glucose (Cerdà et al., 2003). Punicalagins and ellagic acid are responsible for antioxidant activity and healthy benefits of pomegranates (Tyagi, 2012). Punicalagin is inducted in pericarp, husk or seeds. Extraction of punicalagin is 7.6% in water and 7.0% in alcohol. There are differences between amount of ellagic acid (0.2 % in water extraction and 0.4% in alcohol extraction) and punicalagins in pomegranates (Tyagi, 2012).
Content of ellagic acid in pomegranate is different in rind and arils. Amount of ellagic acid is from 2.49±0.1 mg.g\(^{-1}\) to 0.061±0.1 mg.g\(^{-1}\) (Calín Sánchez and Carbonell Barrachina, 2012), but a content of antioxidant is from 0.8 mg.g\(^{-1}\) to 1.8 mg.g\(^{-1}\) (Lee, 2013). Content of ellagic acid in pomegranate is different, because it may depend on a harvest time, ripening of fruits and way of preparing a sample (Lee, 2013). Fresh fruits contain higher concentration antioxidants than treatment fruits - extract or dry samples (Calín Sánchez and Carbonell Barrachina, 2012).

The bioavailability of ellagic acid upon digestion has been debated and reports have described that ellagic acid is metabolised by intestinal microorganisms to form urolithins that are less potent antioxidants but more lipophilic and, therefore, more readily absorbed over the intestinal mucosa into the circulation (Cerdá et al., 2004; Espín et al., 2007). It is well known to have a free radical scavenging activity and has been approved in Japan as an “existing food additive” for antioxidative purposes (Yuan Chiang et al., 2013). Ellagic acid introduces health benefits against cancer, cardiovascular diseases and other disease (Sun et al., 2002). EA can show antitumor effect, induction of cell cycle arrest, apoptosis and inhibition of tumor formation and growth in animals (Seeram et al., 2005). Ellagic acid induced GO/G1 arrest through increase p53 levels and induced apoptosis through activation of caspase-3 activity in human bladder cancer (Li et al., 2005). EA exhibits potent anticancer and antitumor activities towards breast, colorectal, oral, prostate (Losso et al., 2004), pancreatic (Yuan Chiang et al., 2013), bladder (Li et al., 2005), neuroblastoma (Fjæraa Nanberg, 2009), melanoma (Kim et al., 2009) and lymphoma cells (Yuan Chiang et al., 2013). However, there is no evidence regarding the effect of EA on ovarian carcinoma (Yuan Chiang et al., 2013). Recent in vitro evidences revealed that 100µM EA represented little toxic effect on human normal cells (Yuan Chiang et al., 2013).

CONCLUSION
This review describes possible effects of antioxidants compounds of pomegranate on animal cells. Punicalagin and ellagic acid as bioactive phytochemicals have proved influence on apoptosis and proliferation processes. More natural antioxidants have been shown to stimulate the expression of the tumor suppressor gene p53. Ellagic acid has possible positive effect on treatment of various disease - cancer (prostate, breasts, colon, neuroblastoma cells), obesity, cardiovascular disease. In vitro studies are necessary for find out metabolism of ellagitannins and their effect to cell cycle. It is possible, that compounds of pomegranates or their metabolites could have impact on different animal cells and regulate their intracellular mechanism.

Acknowledgments: This work was financially supported by the Ministry of Education, Science, Research and Sport of the Slovak Republic projects no. 1/0790/11, 1/0022/13, APVV-0304-12, and European Community under project no 2622020180. Building Research Centre „AgroBioTech”

REFERENCES


