Anthocyanins present in dietary berries reduce the high androgen production of granulosa cells by interfering with the mitochondrial population and lipid metabolism.

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Infertility is a global health concern affecting 48 million couples and 186 million of persons in the world. Infertility has economic and social consequences for couples who wish to conceive and has been associated with lifestyle factors, including poor diet and physical inactivity. In present-day societies who women choose to have children later in life leads to increase difficulty to conceive by women. The female fertility takes place in ovary, and granulosa cells surrounding the oocyte, support and nurse the developing oocyte. These important cells provide energy for oocyte follicular maturation through carbohydrate, lipid, and protein metabolism, playing an essential role in oocyte maturation and human reproduction. Granulosa cells can be disrupted by environmental factors such pollutants or diets or ageing and addition of anti-stress molecules could improve their activity and the oocyte health.

Numerous basic and clinical studies have demonstrated that micronutrients and more specially, anthocyanins, and other polyphenols from various botanical sources, are efficacious in ameliorating endocrine diseases such as: diabetes or obesity. Some approach by using dietary interventions are used to reduce stress in order to improve fertility outcomes. Several berries characterized by their high content of vitamins, phenolic compounds, and organic acids are used. Blue berries are highly concentrate in anthocyanins which are a bioactive compound, providing many health benefits based on their antioxidant and anti-inflammatory properties, which could improve fertility, and the success in assisted reproductive technology approach.

The objective of our study is to understand at the molecular levels by omics strategy the effect of anthocyanins on human granulosa cells functions. In this study, we have evaluated two varieties of anthocyanidins: delphinidin and aronia extract riched in cyanidin. We assayed proliferative, and steroid production aspects of human GC function.

Granulosa cells exposed to delphinidin have shown that viability are not affected at the 50µM concentration. Expression analysis by RNAseq showed that cholesterol biosynthesis and lipid metabolism pathways are deregulated. The associated lipidomic analyzes confirm a change in lipid profiles with an increase in monosaturated lipids after exposure to delphinidin. One of the consequences is the reduction in steroid synthesis. In addition, anthocyanins reduce the mitochondrial population during long exposure with delphinidin. Seahorse analysis confirm that an acute exposure reduces mitochondrial respiration by 11%. Oxydative stress was evaluated. Delphinidin and aronia extract reduce the Reactive Oxygen Species content in granulosa cells, improving the ageing. However, RNAseq analyzes also showed several pathways associated with the formation of lysosomes that are upregulated. We confirmed by electron microscopic observations that anthocyanin promote autophagy-lysosomal pathway.

In conclusion, delphinidin or Aronia exposition on granulosa will reduce proliferation and limit hyperandrogenism. The beneficial effect of anthocyans on pathological situation (i.e. PCOS) as the ability to slow down their growth, limiting their hyperandrogenism and reducing oxidative stress which suggests an anti-aging effect on the ovarian follicles.

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