Grape stem extracts of Greek *Vitis vinifera* cultivars: Polyhenolic profile and assessment of their anti-angiogenic and anticancer properties

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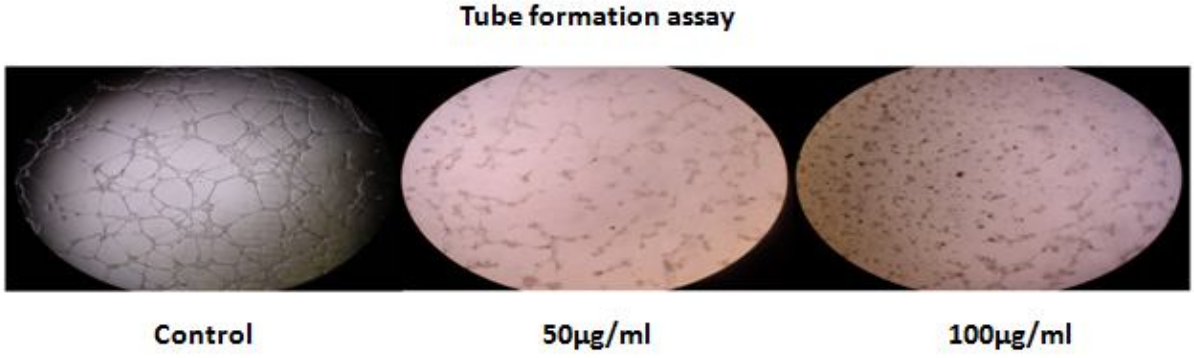
A number of studies have shown that grape extracts exhibit significant anticancer properties, which are associated with their polyphenolic content [1, 2]. Most of these studies refer to grape skins, juices, seeds and pomace. On the other hand, there are no studies concerning the grape stems, a scarcely investigated byproduct produced in large amounts during the vinification process, making the exploitation of grape stems an intriguing research target. Main objective of this endeavor is the assessment of the polyphenolic content of grape stem extracts derived from eight Greek *Vitis vinifera* varieties and the evaluation of their biological properties through the assessment of their effects on liver (HepG2) and cervical (HeLa) cancer cells growth as well as the determination of their *in-vitro* anti-angiogenic properties using the 'tube formation' assay.



In particular, the chemical analysis results indicated that the methanolic extracts of grape stems are particularly rich in polyphenols (flavonoids, phenolic acids and stilbenes), containing noticeable amounts of *trans*-resveratrol (0,33-25,41 mg/g), quercetin (3,94-18,53 mg/g), catechin (2,37-13,75 mg/g), epicatechin (4,51-28,31 mg/g) and ferulic (0,28-11,68 mg/g), gallic (1,52-42,29 mg/g) and syringic (0,80-32,23 mg/g) acids. Additionally, these extracts were found as potent inhibitors of HepG2 (IC_{50}: 34-50 μg/mL) and HeLa (IC_{50}: 15-48 μg/mL) cancer cells growth, at IC_{50} values comparable to those determined for grape seed extracts. Moreover, the white variety Asyrtiko Santorini stems extract was found to inhibit the tube formation (a marker of angiogenesis) by 63% and 94% respectively, in human EAhy926 cells at non-cytotoxic concentrations of 50 and 100 μg/mL. Same extract reduced the expression levels of the main angiogenic factor Vascular Endothelial Growth Factor (VEGF), in EAhy926 cells by 39% at 100 μg/mL, while had no effect on the Hypoxia Inducible Factor-1a (HIF-1a) levels. Thus, the anti-angiogenic potency of the stem extract may be attributed to their capability to inhibit the VEGF through a mechanism that does not involve the HIF-1a.
Results herein suggest that grape stems extracts may account as a rich source of bioactive polyphenols, which display important biological properties.

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