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SCREENING OF 100 PLANT EXTRACTS AS TYROSINASE AND ELASTASE INHIBITORS, TWO ENZYMATIC TARGET OF COSMETIC INTEREST

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Statement of the Problem: Skin ageing processes are generally divided into intrinsic, irremediably tied to the passage of time, and extrinsic, which are caused by environmental factors (i.e. chronic exposure to sunlight, pollutants) and miscellaneous lifestyle components. Plants are a precious resource for skincare, both as antioxidants and inhibitors of enzymes involved in the ageing process. In this context, elastase and tyrosinase are target of remarkable importance, and their inhibitors find applications as skin whitening, anti-wrinkle, anti-sagging agents, and in the treatment of dermatological disorders.

Methodology: The plant sources were from: India (Rajasthan), Africa (Burkina Faso) and Mediterranean area. Hydroalcoholic extracts were prepared, dried and dissolved in water for the assays or in water-d₂ phosphate buffer (90 mM; pH 6.0) for ¹H-NMR analysis.

Findings: 17 plants resulted to be endowed with strong bioactivity and leaves of *Pistacia lentiscus* emerged as the most potent sample on both enzymes (IC₅₀ of 7.18 ±1.37 and 42.04±1.94 µg/mL against elastase and tyrosinase, respectively). Interestingly, two, out of the 17 most active plants, are endemic of Sardinia Island (Italy), namely: *Hypericum scruglii* and *Limonium morisianum*. Moreover, the 17 most active extracts resulted also generally enriched in polyphenols and flavonoids, which confer them additional value, due to their antioxidant potential. Lastly, ¹H NMR metabolomics profile of the extracts were measured, compared by multivariate data analysis and correlated to the abovementioned results by orthogonal projections to latent structures (OPLS) model, showing a positive correlation between spectral signal of aromatic compounds and the potency of enzymatic inhibition.

Conclusion & Significance: This bio-screening allowed the selection of 17 plant extracts, promising as cosmetic ingredients, which safety is also supported by the ethnobotanical uses. Nine of them proved active both against

tyrosinase and elastase and as shown by the OPLS model their aromatic phytoconstituents play a key role in conferring these bioactivities.

Recent Publications

1. Liyanaarachchi G D, Samarasekera J K, Mahanama K R and Hemalal K D (2018) Tyrosinase, elastase, hyaluronidase, inhibitory and antioxidant activity of Sri Lankan medicinal plants for novel cosmeceuticals. *Industrial Crops and Products* 111:597–605.
2. Pillaiyar T, Manickam M and Namasivayam V (2017) Skin whitening agents: medicinal chemistry perspective of tyrosinase inhibitors. *Journal of Enzyme Inhibition and Medicinal Chemistry* 32:403–25.
3. Imokawa G and Ishida K (2015) Biological mechanisms underlying the ultraviolet radiation-induced formation of skin wrinkling and sagging I: reduced skin elasticity, highly associated with enhanced dermal elastase activity, triggers wrinkling and sagging. *International Journal of Molecular Sciences* 16:7753–7775.
4. Mukherjee P K, Maity N, Nema N K and Sarkar B K (2011) Bioactive compounds from natural resources against skin aging. *Phytomedicine* 19:64–73.
5. Yuliana N D, Khatib A, Choi Y H and Verpoorte R (2011) Metabolomics for bioactivity assessment of natural products. *Phytotherapy Research* 25:157–69.

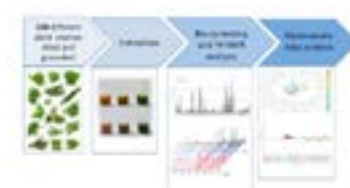


Fig. 5: Schematic representation of the workflow. (1) Plant material extraction and preparation; (2) Tyrosinase and Elastase assays; (3) Bioactivity and chemical analysis; (4) OPLS model analysis.

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Biography

Manuela Mandrone works at Bologna University, Department of Pharmacology and Biotechnology, where she is a Junior Researcher since 2016. Her investigations are in the field of Plant Science, particularly focusing on natural-product based drug discovery inspired by traditional medicine knowledge and studies of plant-environment interactions, related to crops. She has expertise in identification of active principles responsible for biological activities of medicinal plants, finding of biomarkers and quality control of botanicals. These lines of research lie on canonical phytochemical studies as well as on novel approaches such as: metabolomics coupled with chemometrics, which has been a subject of her PhD thesis. She also has expertise in biological activities screening, antioxidant and enzymatic inhibitory assays.

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