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in silico prediction of the skin biological activity for botanical active ingredients based on their composition in phytocomponents

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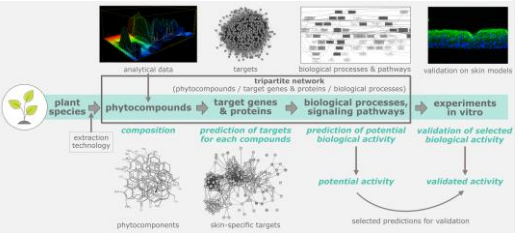
Introduction

The combination of analytical approaches to finely characterize the composition in active phytocomponents constituting a botanical extract, with bioinformatics allows the prediction of potential target genes and the identification of subsequent potential biological activities prior to realizing any experiment in-vitro.
This Network Pharmacology approach can be applied to botanical extract in order to predict their potential activity that can be further validated by in vitro experiments of skin models.

Methods

Network pharmacology links phytocomponents to human target genes and proteins and helps predict biological activity.
Thereby, this type of study relies on the analytical determination of the major components of a botanical extract.
The next step is the determination of validated relationships (scientific literature, databases, and experimental data) associated with the prediction of undescribed but potential connections (*e.g., via* structural biology approaches) leading to a list of targets that will serve as a base for gene enrichment studies, to point out specific associated biological processes and pathways of interest.
The output can be represented as a tripartite "active phytocompound / target proteins & genes / biological activity & signaling pathway" set of data that can be used as a predictive ground to further perform experimental validation on dedicated skin models.
In this study we present the application of network pharmacology to the prediction of the skin biological activity of a particular botanical extract.



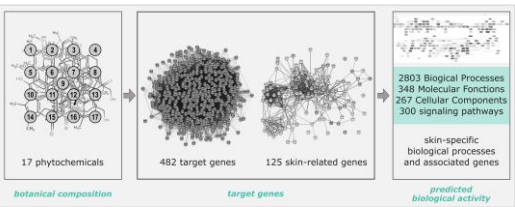
Workflow of the studies leading to the prediction of the biological activity of a plant extract with defined composition

Results

Network pharmacology approach for sandalwood extract

Network pharmacology analysis was used to predict the potential skin biological activity.
First, a compound-target network was established via virtual screening based on similarity structure prediction combined with literature and database mining.
Second, the curated compound-target network resulting in a total of 482 genes, served as a base to gene and pathway enrichment studies, an approach that allows to discover hidden patterns within large amounts of data. This led to the identification of 2803 biological processes, 348 molecular functions and 267 cellular components, and more than 300 signaling pathways.
The identification of 125 skin-related genes within the initial 482 genes, allowed to focus on the prediction of skin-related potential activities and modulated pathways.

Due to its predictive potential, Bioinformatics can improve the success rate and speed-up the process of active ingredient development.
Indeed, this approach allows to dig into large datasets to detect hidden patterns and draw predictions that only the machine can discern.

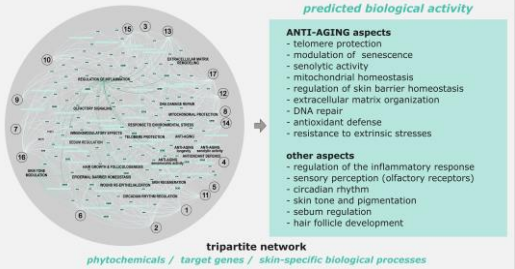


Network pharmacology approach for sandalwood extract.

Seventeen major chemical compounds were identified, and the potential target genes were predicted. Hence, 482 targets were pointed-out, with 125 among them being more specific of the skin tissue. Gene enrichment analysis led to the discovery of associated biological processes, molecular functions and cellular components, together with signaling pathways that could be involved.

Tripartite network representation of the results

The enrichment analysis led to the identification of hidden patterns corresponding to potential biological activities in relation with specific subsets of genes.
The main predicted aspects (telomere protection, modulation of senescence, senolytic activity, mitochondrial homeostasis, regulation of skin barrier homeostasis, extracellular matrix organization, DNA repair, antioxidant defense, resistance to extrinsic stresses) were found to be related to anti-aging.
Other aspects corresponded to the regulation of the inflammatory response, sensory perception (olfactory receptors), circadian rhythm, skin tone and pigmentation, sebum regulation, and hair follicle development.
A tripartite network comprising the seventeen phytochemicals in interaction with predicted target genes and subsequent biological activity was built to summarize the study.



Tripartite network.

The relationships between phytoconstituents of the sandalwood extract, the predicted target genes and the associated biological activities are represented. The main aspects of the predicted activities are listed.

Conclusion

Network pharmacology is evolving as a systematic paradigm and becoming a frontier research field of active ingredient discovery and development.
The ability to predict the biological activity in-silico prior to any laboratory experiment corresponds to a virtual screening of the potential activity and leads to a gain in efficacy and allows to save time and resources.
The predictions can be used to orient the strategy of the experimental validation in-vitro, according to expected benefits and positioning of the botanical extract in development.