

# UNTARGETED METABOLOMIC PROFILING OF SKIN REVEALS POTENTIAL BENEFITS OF AN EXTRACT OF MYROTHAMNUS FLABELLIFOLIA, THROUGH AN IMPACT ON BIOLOGICAL PROCESSES IMPLICATED IN SKIN AGING

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## 1 INTRODUCTION

The process of skin aging in humans is complex and is induced by multiple factors, including genetic (intrinsic) and various environmental (extrinsic) ones.

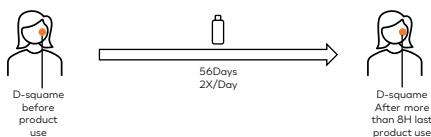
Untargeted metabolomics is emerging as a powerful tool to understand the aging process at a molecular level. Power of metabolomics can be utilized to understand the metabolic changes in human skin aging, both as drivers of functional deterioration as well as a target for anti-aging treatments and if the treatment has a beneficial effect on skin.

Here, we evaluated biochemical changes on skin of 30 individuals after application with a formulation containing an extract from desiccation tolerant medicinal herb, *Myrothamnus flabellifolia*, using untargeted metabolomics analysis at baseline (D0) and post- application (D56).

## 2 MATERIALS & METHODS

The study included facial skin metabolome analysis of 32 Asian women, 45 to 60 years old, representing all skin types and living in Singapore. They were showing signs of aging (wrinkles, spots, etc.), living in a polluted environment an answered to "Urban lifestyle" questionnaire for recruitment of the panel. The air quality and ozone index were monitored. They followed a 15-day wash out with a neutral cream. The women applied the formulation containing *M. flabellifolia* twice a day for 56 days.

D-Squam sampling on the cheek was done on D0 & D56 for untargeted metabolomics analysis that was performed at Metabolon, Inc (Morrisville, NC, USA).



In brief, samples were extracted and split into equal parts for analysis on the LC/MS/MS and Polar LC platforms.

Proprietary software was used to match ions to an in-house library of standards for metabolite identification and for metabolite quantitation by peak area integration. Matched pairs t-test, Random Forest Analysis (RFA), and Principal Component Analysis (PCA) were used to analyze the data. We also carried out metabolite profiling of *M. flabellifolia* extract and did a comparative analysis of plant metabolites and skin metabolite pathways.

Matched pairs t-test was used to determine whether the means of two populations were different.

p-value: evidence that the means are different (smaller is better)

q-value: estimate of the false discovery rate (smaller is better)

ps<0.05 was taken as significant

Sub Pathway	Biochemical Name	Fold of Change	
		Matched Pairs t-Test	
		D56	D0
Pentose Metabolism	ribonate	1.37	
	arabinose	0.64	
	arabitol	2.81	
	arabonitriloxylol	1.11	
	inonate	0.54	
Disaccharides and Oligosaccharides	galactose	1.25	
	sucrose	1.51	
	trehalose	2.01	
	mannitol/sorbitol	3.62	
	mannitol/sorbitol	1.82	

**0.55** Green: indicates significant difference (ps<0.05) between the groups shown; GREEN indicates a ratio < 1  
**1.71** Red: indicates significant difference (ps<0.05) between the groups shown; RED indicates a ratio > 1  
**0.65** Light green: narrowly missed cutoff for significance; 0.05<p<0.10; light green indicates a ratio < 1  
**1.80** Light red: narrowly missed cutoff for significance; 0.05<p<0.10; light red indicates a ratio > 1  
**1.20** Non-colored text and cell: mean values are not significantly different for that comparison

## REFERENCES

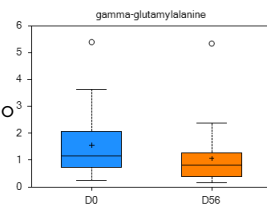
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## 3 RESULTS & DISCUSSION

Between all the tested samples, a total of 548 biochemicals (456 named and 92 unnamed) were found in this study. These biochemicals were then examined across the treatment group relative to baseline levels to elucidate metabolomic profiles of treatment response.

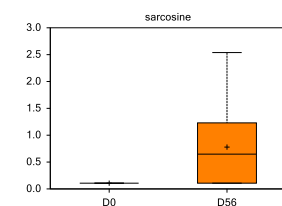
### VARIATION ON SKIN HYDRATION KEY METABOLITES

In volunteers treated with the product formula for 56 days, it was found significantly less amino acids, peptides and gamma-glutamyl amino acids and less degradation of protein.

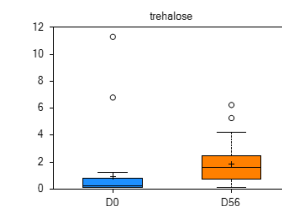


The osmolytes betaine and sarcosine were increased in subjects following treatment :

Biochemical Name	Fold of Change	
	Matched Pairs t-Test	
	D56	D0
sarcosine	7.28	
betaine	6.36	
mannitol/sorbitol	3.62	

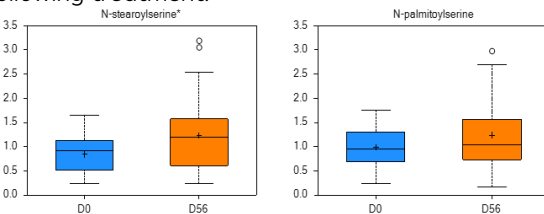


Several sugars (e.g. arabinol, sucrose, trehalose, and erythronate) were increased in treated volunteers, those sugars were also present at high levels in the *Myrothamnus flabellifolia* extract and formula containing the extract



### LIPID-RELATED CHANGES IN SKIN

Fatty acid ethanolamides, also referred to as endocannabinoids, are bioactive lipids that are involved in a wide range of cell signaling and biological activities in various tissues, including skin. Here, there was a trend of significant increases in endocannabinoids following treatment.



## 4 CONCLUSION

Overall, the results demonstrated post-application metabolomic signatures including elevated osmolyte levels, fatty acid levels and metabolism change. These changes can improve skin hydration, barrier function and limited skin tightness. [1-5]

Moreover, a first knowledge study had highlighted that skin regularly exposed to a polluted environment was linked to a high level of gamma-glutamyl amino acids which would indicate a compromised barrier function. [6] Our results, put into perspective with this study, indicate a decrease in the level of gamma-glutamyl amino-acids, then a maintenance of the barrier function with the use of the product despite a polluted environment.

Collectively, the findings suggest that the tested skincare treatment plays a significant role in mediating skin functions that are important to consider for the prevention of skin aging.