

VICHY THERMAL SPRING WATER (VTSW), A COSMETIC INGREDIENT OF POTENTIAL INTEREST IN THE FRAME OF SKIN AGEING EXPOSOME

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INTRODUCTION

The major environmental factors that influence skin ageing have been recently grouped in the so-called skin ageing exposome which includes sun radiations, air pollution, tobacco smoke, nutrition, and other factors such as temperature, stress and lack of sleep. Considering the age- and exposome-related alterations of skin structure and functions, one might consider that various cations contained in VTSW (Table 1) could be of help to restore proper skin homeostasis and function.

Table 1: Composition and characteristics of VTSW

Resistivity	134 ohm.cm
Osmolarity	171 mOsm kg ⁻¹
Hydrogencarbonates (HCO ₃ ⁻)	4.818,633 mg L ⁻¹
Orthophosphate (PO ₄ ⁻³)	0.210 mg
Sulphate	182.39 mg L ⁻¹
Boron	0.970 mg L ⁻¹
Calcium	165.61 mg L ⁻¹
Iron	0.810 mg L ⁻¹
Fluorine	7.67 mg L ⁻¹
Lithium	5.17 mg L ⁻¹
Magnesium	12.08 mg L ⁻¹
Potassium	103.56 mg L ⁻¹
Silicon	11.78 mg L ⁻¹
Sodium	1862.88 mg L ⁻¹
Strontium	1.63 mg L ⁻¹
Iron	0.810 mg L ⁻¹
Manganese	0.208 mg L ⁻¹
Resistivity	134 ohm.cm
Osmolarity	171 mOsm kg ⁻¹

Objective

Skin ageing is clinically well characterized and results from the cumulative effects of chronological ageing and environmental factors. Skin undergoes histological modifications as a result of an altered balance between keratinocyte proliferation and differentiation. VTSW being characterized by a very high minerality and a specific ionic composition, its effects on human keratinocytes grown *in vitro* has been characterized.

MATERIALS AND METHODS

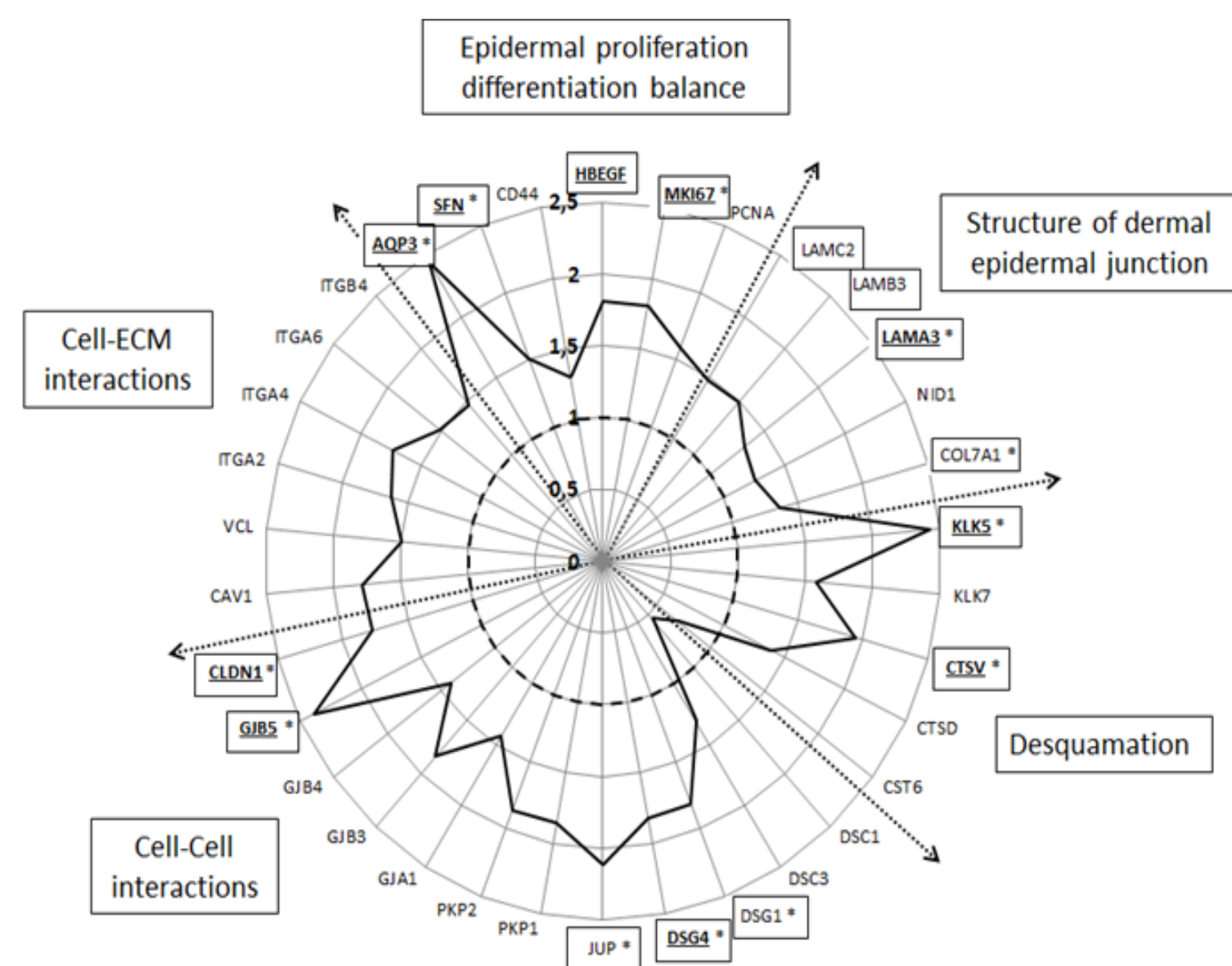
Human keratinocytes were grown *in vitro* in the presence or absence of VTSW, and a full genome gene expression profiling was established with Affymetrix Human Gene 2.0 ST. Only genes presenting a fold change value |FC| ≥ 1.5 and a P Value < 0.05 were selected, as differentially expressed. In parallel, the effect of VTSW on the *in vitro* expression of keratinocyte late differentiation markers was studied by immunofluorescence, in comparison with Ca²⁺.

RESULTS

1/ Gene expression profiling.

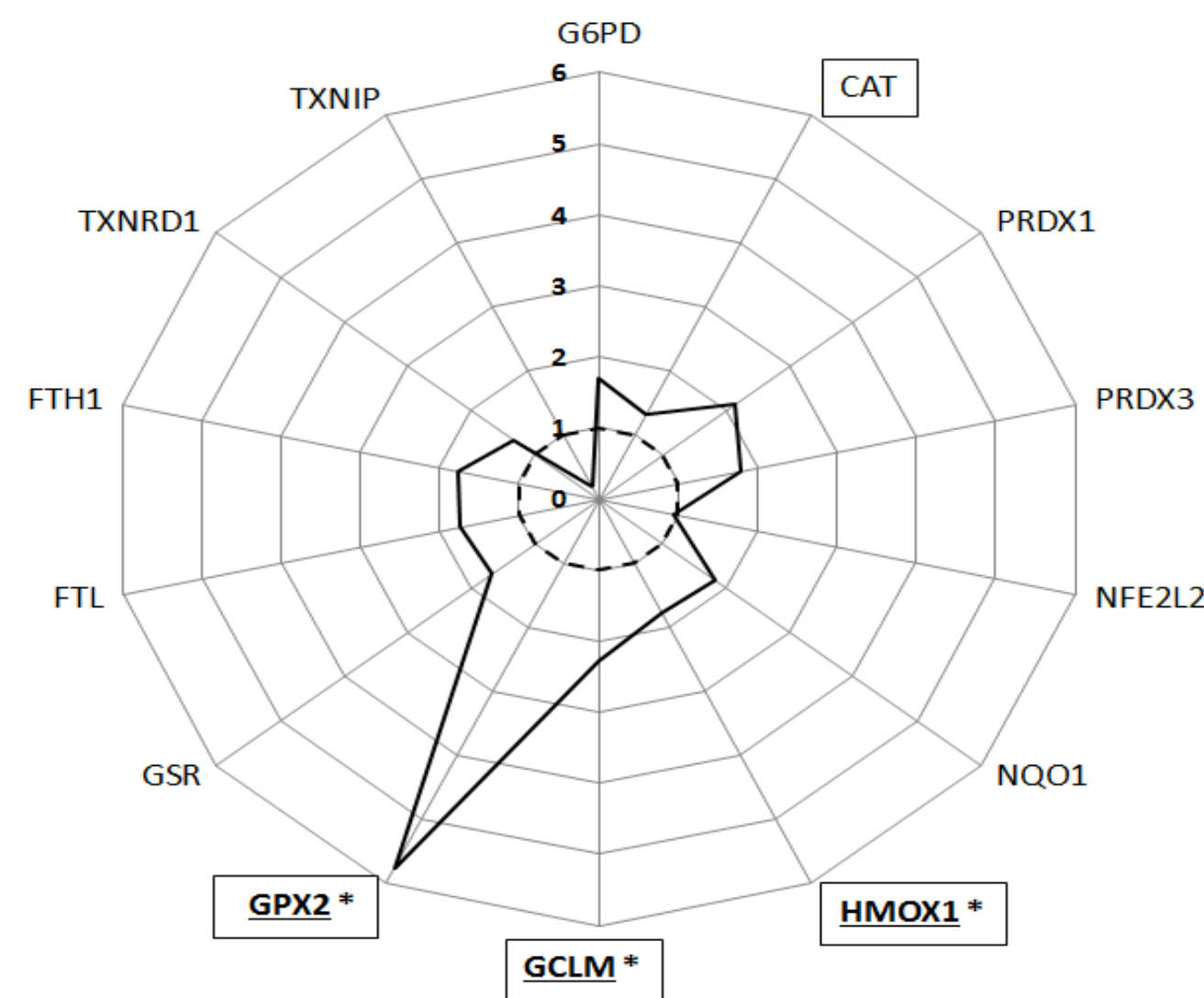
In the presence of 50% of VTSW, the expression of numerous genes is modulated: a functional analysis with biological functions enrichment algorithm highlights 79 genes differentially expressed and mainly clustered in functional groups, which cover main processes involved in skin homeostasis, specifically with respect to dermal-epidermal junction, epidermal cohesion and communication, keratinocyte proliferation–differentiation balance, antioxidant mechanisms (Figures 1 and 2).

Figure 1: Impact of VTSW on epidermis structure-related gene expression



The expression of a set of 34 genes was found modified. The gene expression ratio between VTSW treatment and the untreated control are represented with the continuous line. The dashed line is the baseline representing no expression modulation (ratio = 1). Genes squared have been checked with RT-PCR: (i) bold and underline for genes with ratio ≥ 1.5 or ≤ 0.67. (ii) *: pV < 0.05.

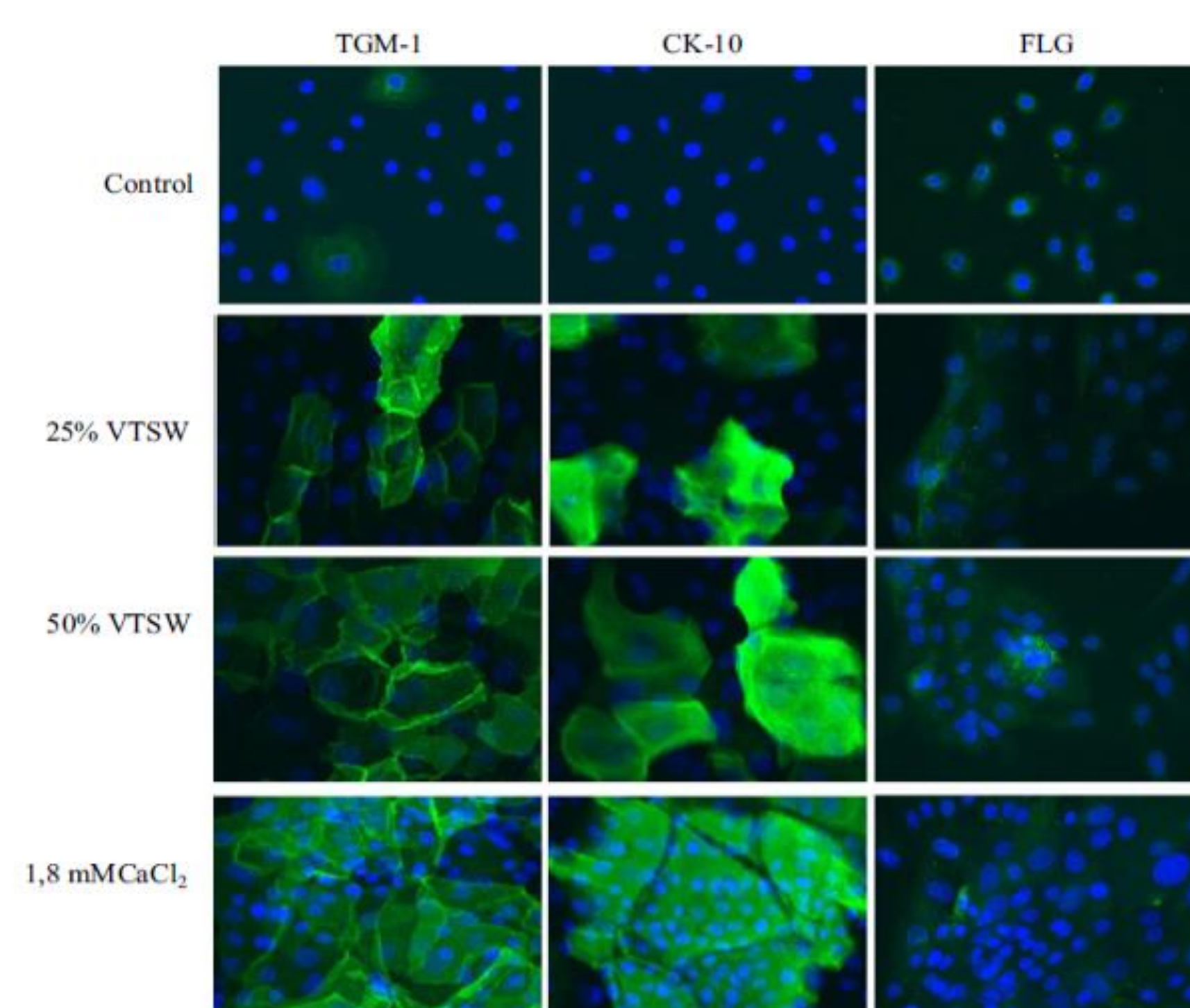
Figure 2: Response to oxidative stress –VTSW 18h



The expression of a set of 14 genes was found modified. They are linked to the oxidative stress response, more specifically to the Nrf2 pathway, the redox status, and iron storage. The gene expression ratio between VTSW treatment and the untreated control are represented with the continuous line. The dashed line is the baseline representing no expression modulation (ratio = 1). Genes squared have been checked with RT-PCR: (i) bold and underline for genes with ratio ≥ 1.5 or ≤ 0.67 (ii) *: pV < 0.05.

2/ Immunofluorescence.

Figure 3: Effect of VTSW vs CaCl₂ on 3 differentiation markers



Immunofluorescence detection of 3 keratinocyte differentiation markers: TGM-1, CK-10, FLG. VTSW ionic mix shows a stronger effect in a dose-dependent manner than CaCl₂ alone.

Transcriptomic results indicated that VTSW may modulate the proliferation–differentiation balance in keratinocytes, by stimulating the terminal differentiation pathway. To further characterize this effect, VTSW was compared to Ca⁺⁺, a well-known epidermal differentiation factor. Immunofluorescence detection demonstrated that the VTSW ionic mix has a stronger effect than CaCl₂ alone on these 3 keratinocyte differentiation markers: TGM-1 (*transglutaminase 1*), CK-10 (*keratin 10*) and FLG (*filaggrin*) (Figure 3).

CONCLUSION

The expression of a set of genes is modulated in keratinocytes grown in the presence of 50% VTSW, mainly involved in skin homeostasis, skin ageing and response to skin ageing exposome. These coordinated and integrated responses to VTSW might be linked to the key role(s) of cations in regulating and co-activating a whole array of epidermal functions which are altered during skin ageing and by skin exposome. This work suggests that Vichy Thermal Spring Water could be considered as an ingredient of potential interest to address some of the deleterious effects of skin ageing exposome.