

NIHON KOLMAR CO.,LTD.

The innovative approach to develop cosmetics for sensitive skin: the relation between preservatives and inflammatory cytokines

Poster ID
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Introduction:

Although preservatives are essential ingredients to maintain the quality of cosmetic products, these are considered to be one of the causes of skin irritation. In the IFSCC 2020 Yokohama Congress, we reported that several preservatives, such as phenoxyethanol, increase the levels of inflammatory cytokines in our skin. On the other hand, many ingredients, which have antibacterial effects and are not listed as preservative on the positive list of cosmetic standards, are used in most cosmetics for sensitive skin. However, there are no reports investigating the expression of inflammatory cytokines induced by these ingredients. Thus, we examined the inflammatory cytokines induced by preservatives commonly used in cosmetics worldwide and their alternatives. Furthermore, we evaluated anti-inflammatory cytokine and how these ingredients affect the epidermal differentiation.

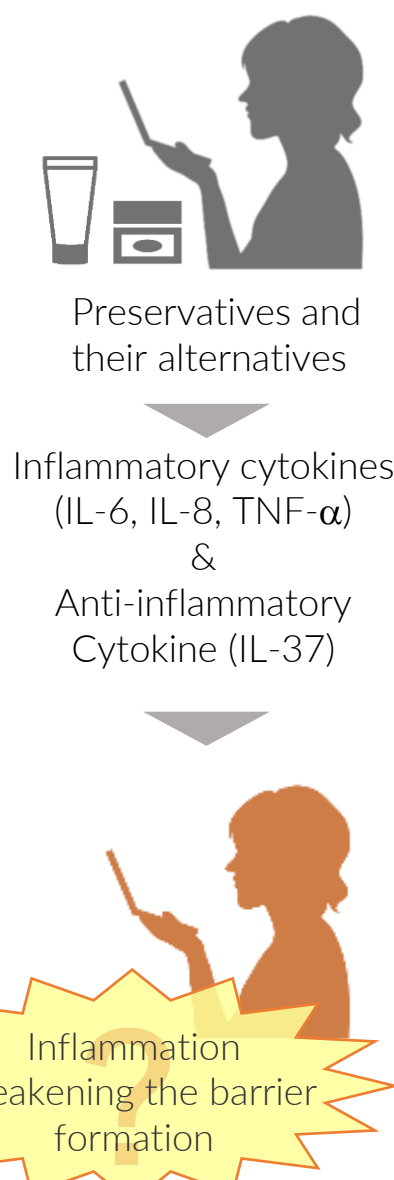
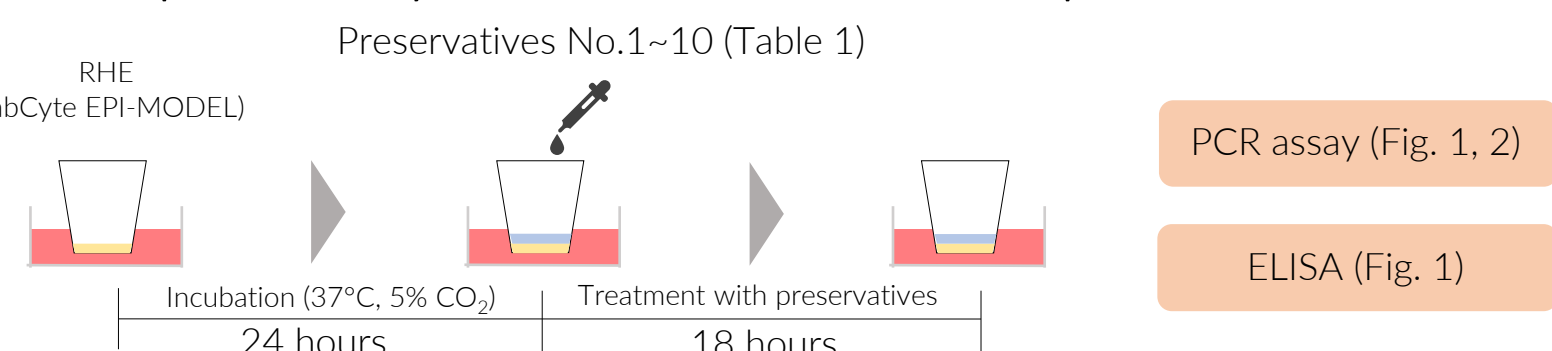


Table 1. 15 preservatives and their alternatives

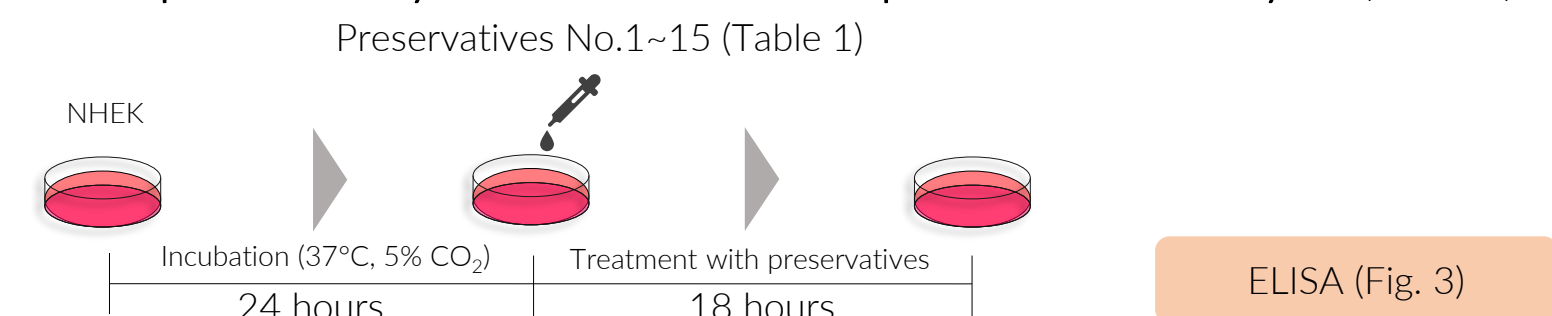
1	Potassium Sorbate (POT)	9	Butylparaben (BUT)
2	Caprylyl Glycol (CAP)	10	Propylparaben (PRO)
3	Sodium Benzoate (SOD)	11	Methylparaben (MET)
4	Bisabolol (BIS)	12	Pentylene Glycol (PEN)
5	Butylene Glycol (BUG)	13	1,2-Hexanediol (HEX)
6	Benzyl Alcohol (BEN)	14	Ethylhexylglycerin (ETH)
7	Glyceryl Caprylate (GLY)	15	Phenoxyethanol (PHE)
8	Ethylparaben (ETP)		

Materials & Methods:

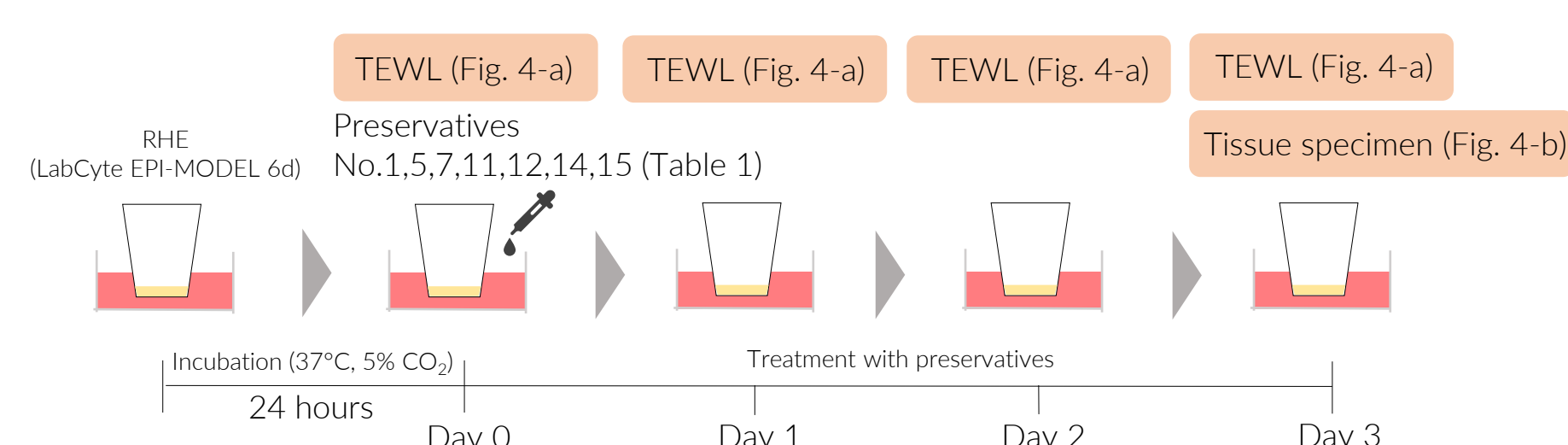
A. Gene and protein assay with a reconstructed human epidermis (RHE)



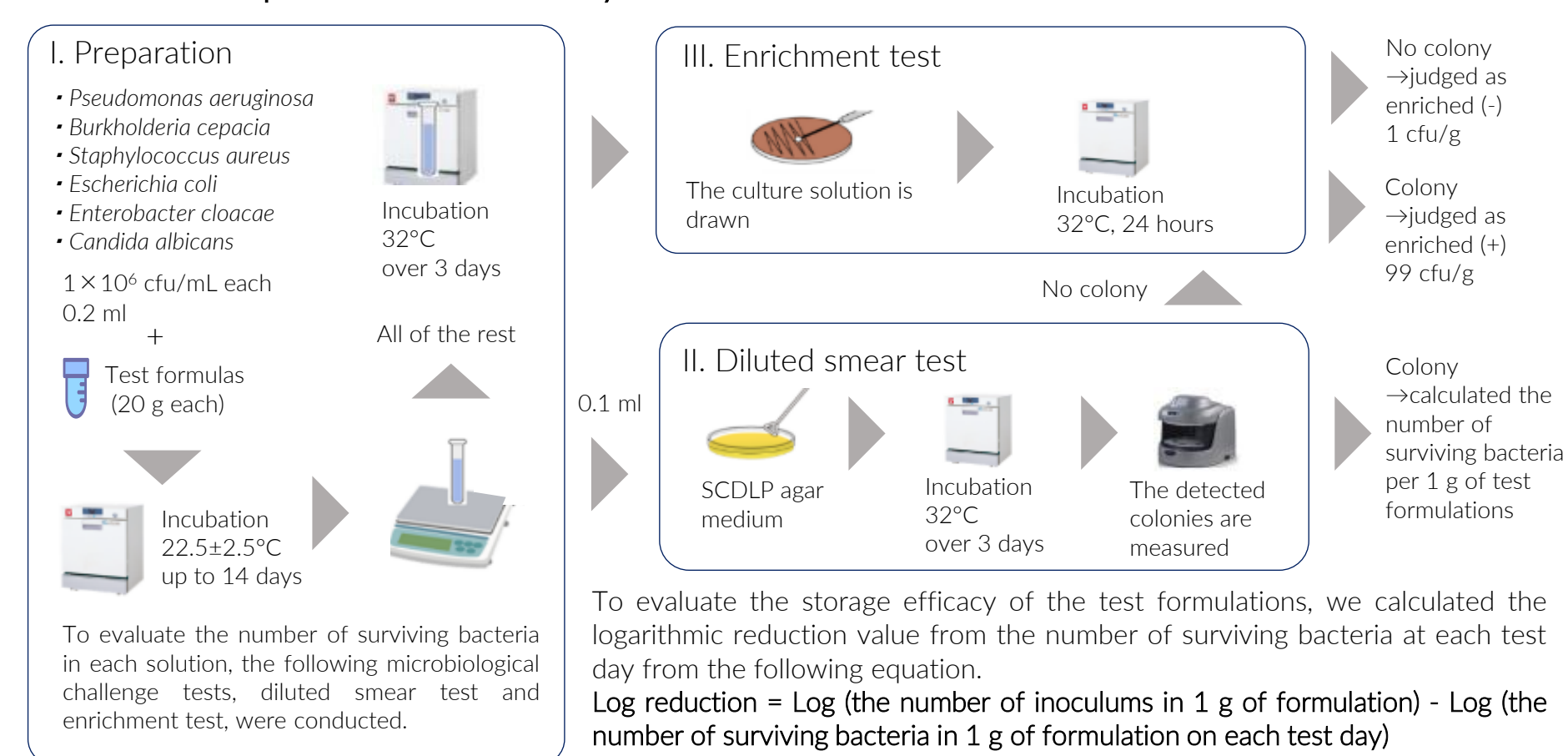
B. Gene and protein assay with normal human epidermal keratinocytes (NHEK)



C. Effects of preservatives in an immature RHE model



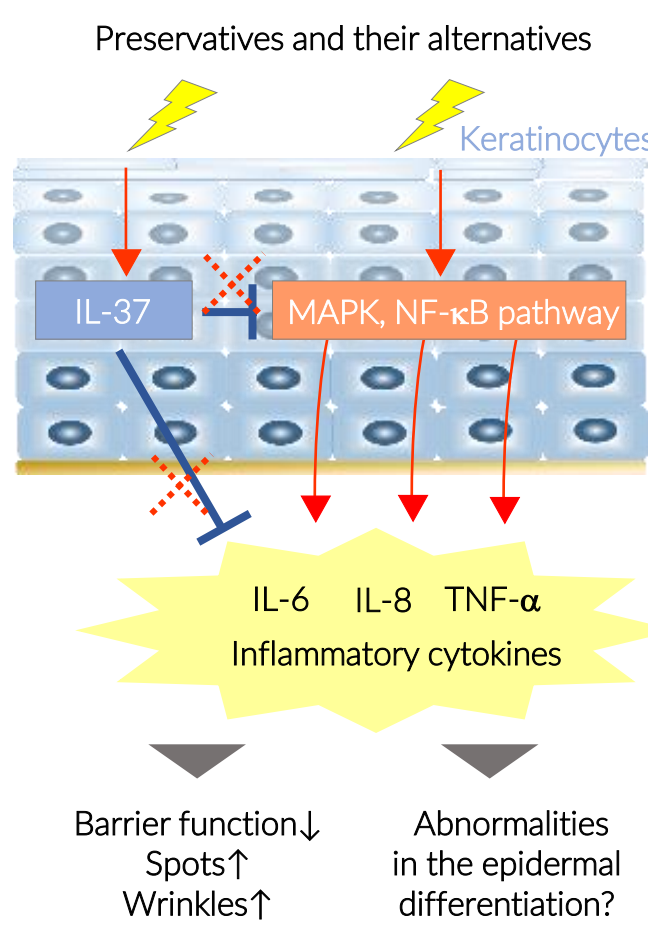
D. The test of preservative efficacy



As an evaluation standard, a test formulation in which the number of bacteria decreased by 2.5 Log or more on the 7th day or the number of bacteria decreased by 3.5 Log or more on the 14th day was judged to have enough antimicrobial effect as a cosmetic product.

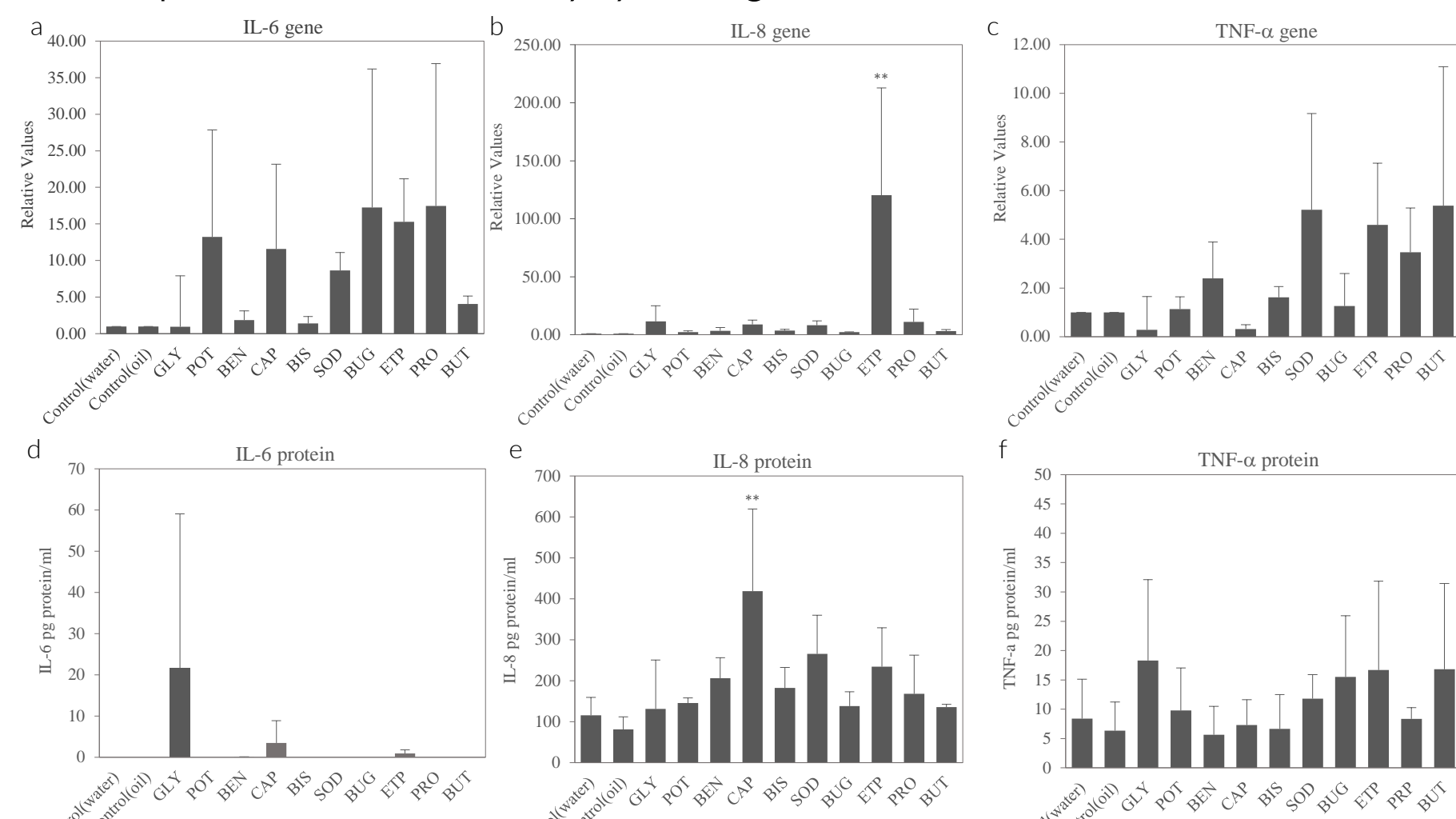
Conclusions:

- The expressions of inflammatory cytokines were different depending on preservatives. There were also differences between RHE and NHEK, which is thought to be affected by the difference in permeability.
- CAP, SOD, ETP, BUT, PRO, BIS, BUG, and GLY significantly decreased the expression of IL-37, suggesting that these inflammatory response might be affected by anti-inflammatory response.
- BUG and PEN had enough antimicrobial efficacy as cosmetics without inducing inflammatory cytokines.
- The combination of POT, BIS and BEN might be a good option to develop cosmetics for sensitive skin.
- Preservatives and their alternatives caused abnormalities in the epidermal differentiation.
- To sum up, preservatives and their alternatives should be selected carefully, even though the alternatives are not defined as preservatives.

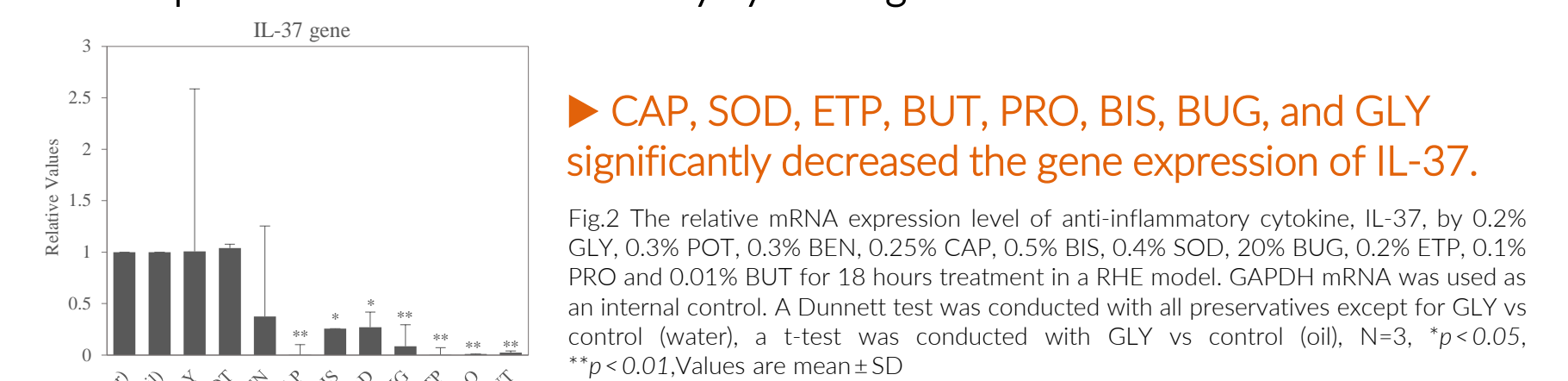


Results & Discussion:

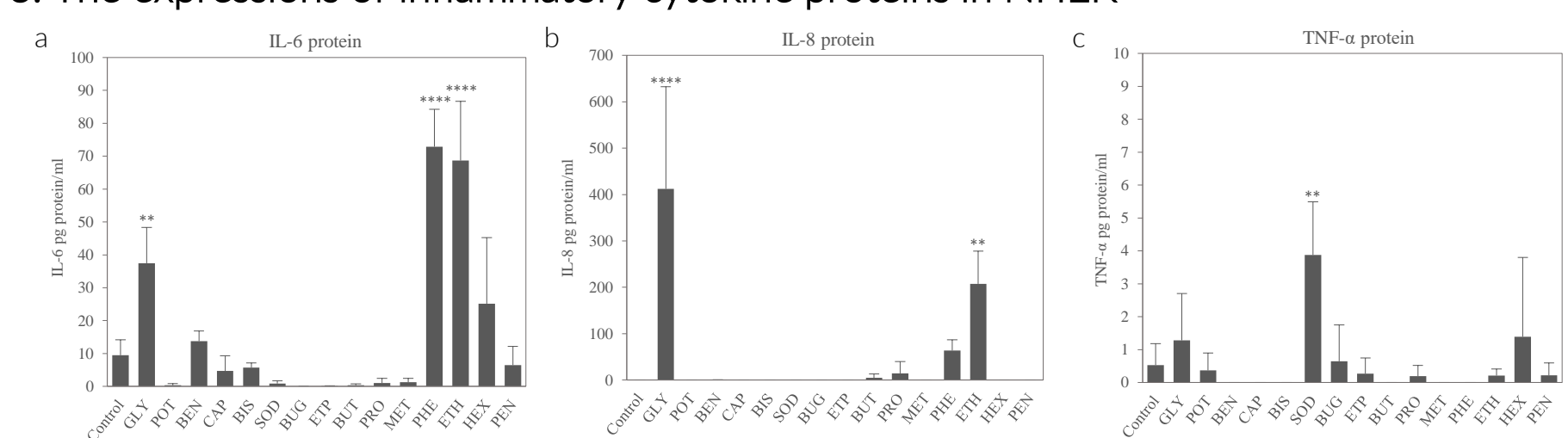
1. The expressions of inflammatory cytokine genes in a RHE model



2. The expressions of anti-inflammatory cytokine gene in a RHE model



3. The expressions of inflammatory cytokine proteins in NHEK



4. The antimicrobial efficacy and the summary of inflammatory cytokines expressions

Table 2. The results of the antimicrobial efficacy test and the summary of expressions of inflammatory cytokines which had significant increase by each preservative and its alternative for 18 hours treatment in NHEK and RHE models, *p<0.05, **p<0.01, ****p<0.0001, vs control, Dunnett

	The antimicrobial efficacy					The summary of inflammatory cytokines expressions								
	Concentrations (%)	Log reduction			Result	IL-6			IL-8			TNF-α		
		Day0	Day7	Day14		gene (RHE)	protein (RHE)	protein (NHEK)	gene (RHE)	protein (RHE)	protein (NHEK)	gene (RHE)	protein (RHE)	protein (NHEK)
Standard	-	0	2.5	3.5	-									
Potassium Sorbate (POT)	0.3	0	0	0	Fail									
Caprylyl Glycol (CAP)	0.25	0	3.8	6.1	Pass				**					
Sodium Benzoate (SOD)	0.4	0	0	0	Fail									**
Bisabolol (BIS)	0.5	0	0	0	Fail									
Butylene Glycol (BUG)	20	0	6.1	-	Pass									
Benzyl Alcohol (BEN)	0.3	0	1.5	1.6	Fail									
Glyceryl Caprylate (GLY)	0.2	0	6.1	-	Pass			**			****			
Ethylparaben (ETP)	0.2	0	6.1	-	Pass				**					
Butylparaben (BUT)	0.1	0	6.1	-	Pass									
Propylparaben (PRO)	0.01	0	6.1	-	Pass									
Methylparaben (MET)	0.2	0	4.1	6.1	Pass				*					
Pentylene Glycol (PEN)	5	0	3.2	6.1	Pass									
1,2-Hexanediol (HEX)	1	0	1.9	2.4	Fail				*					
Ethylhexylglycerin (ETH)	0.05	0	0.8	0	Fail			****	*		**			
Phenoxyethanol (PHE)	0.5	0	2.4	5.2	Fail		*	****	*					

- BUG and PEN had enough antimicrobial efficacy as cosmetics without inducing inflammatory cytokines.
- The combination of POT, BIS and BEN might be a good option to develop cosmetics for sensitive skin.
- ETP, BUT and PRO contained 20% BUG and 4% Ethanol to dissolve in water and could not be conducted at the typical concentrations in cosmetics.

5. Effects of preservatives in an immature RHE model

