32nd IFSCC Congress
London 19-22 September 2022

COSMAX BTI

Poster ID 294

Oil extracted from extremophile *Yarrowia lipolytica* alleviates the cold stress-induced skin aging

Kyung, Seoyeon[1]; Lee, Eun-Jung[1]; Kim, Minji[1]; Nam, Jin Ju[1]; Nho, Youn-Hwa[1]; Ryu, Jeoungjin[1]; Park, Myeong Sam[2]; Kang, Seunghyun[1]*;*

[1]COSMAX BTI, 255 Pangyo-ro, Bundang-gu, Seongnam-si, Gyeonggi-do, 13486, Republic of Korea
[2]COSMAX R&I Center, 255 Pangyo-ro, Bundang-gu, Seongnam-si, Gyeonggi-do, 13486, Republic of Korea

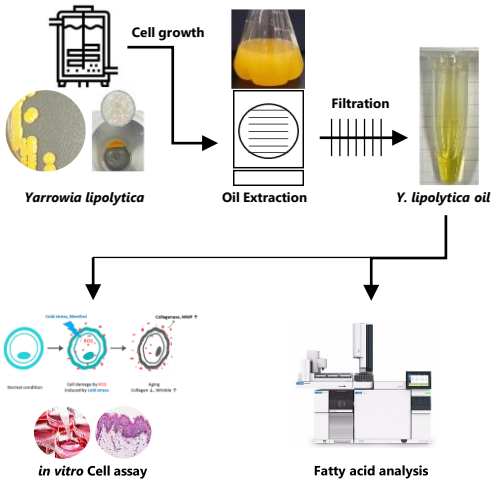
Introduction:

The seasonal and climatic cold conditions would be the one of critical causative factors of skin aging and skin barrier abnormalities including the dry and sensation of itchy [1]. Especially for those who work in cold environments or where being outside in cold temperatures with lengthy exposures can cause dry skin conditions or aggravate common dermatoses, such as atopic dermatitis and psoriasis [2]. Cold conditions represent an environmental factor, where facial cooling usually occurs within minutes, contributing to skin sensitivity. Thus, cold weather appears to be a major concern of potential skin irritation [3]. These researches highlighted the importance of the understanding of the effects of cold condition on skin barrier and skin aging.

Cold-inducible RNA-binding protein (CIRP) is identified as a cold-shock protein that is upregulated in response to hypoxia, oxidative stress as well as hypothermia stress. The CIRP is known to be activated by the cold temperature or menthol, a substitute that causes cold stress, via transient receptor potential melastatin 8 (TRPM8) channel [4, 5]. TRPM8 is known to mainly function for sensory responsiveness to cold temperature in neuron and also expressed in epidermal keratinocytes as functioning skin homeostasis [6]. Cold exposure in humans is also known to increase oxidative stress [7, 8]. Menthol was known to activate CIRP via TRPM 8 channel, a major sensor of environmental cold temperatures. In our previous study (not published yet), collagen type XVII (COL17), which was known to facilitate the keratinocyte adhesion and to be located at the basement membrane, which thins and flattens with increasing ages, were down-regulated under cold treatment mimicked by menthol.

Oleaginous yeast *Yarrowia lipolytica* (*Y. lipolytica*) has found in natural ecosystems as well as the extreme environments, such as arctic, antarctic sea, and so on [9]. This extremophile yeast has emerged both as a convenient microorganism for industrial application and as a model organism for investigating oil synthesis and accumulation in microbes and higher organisms [10]. Because it is recognized as a generally regarded as safe (GRAS) microorganism, their application field has been also expanded to cosmetic industry.

Materials & Methods:



Results & Discussion:

In this study, we aimed to develop the new cosmetic ingredients to prevent skin aging caused by cold stress.

To examine the effect of oil obtained from *Y. lipolytica* under the cold stress condition, we checked the expression levels of several marker genes related to skin aging. *Y. lipolytica* oil up-regulated the expression of SOD2 and COL17 genes in cold stress induced human keratinocytes (**Fig 1&2**).

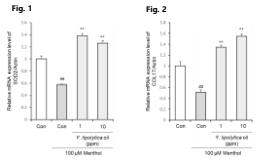


Fig. 1. Relative expression level of SOD2 under the treatment of oil extracted from *Y. lipolytica* in human keratinocytes.
Fig 2. Relative expression level of COL17 in the presence of oil extracted from *Y. lipolytica* in human keratinocytes.
##p<0.01 indicates a significant difference from the menthol-treated control. ***p<0.01* indicates a significant difference from the control.

Collagen synthesis is decreased and matrix metalloproteinase-1 (MMP-1) level is increased under the UVB irradiation. *Y. lipolytica* oil alleviated the increase in MMP-1 expression and the decrease in procollagen synthesis by UVB irradiation in human keratinocytes (**Fig 3&4**). It indicated that *Y. lipolytica* oil improved the skin anti-aging markers *in vitro*.

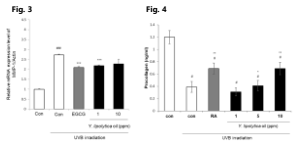


Fig. 3. Relative expression level of MMP-1 in the presence of oil extracted from *Y. lipolytica* in human keratinocytes. EGCG was used for positive control. *##p<0.001* indicates a significant difference from the control. ****p<0.001* indicates a significant difference from the UVB-irradiated control.
Fig 4. The contents of procollagen under the treatment of *Y. lipolytica* oil in UVB-irradiated human keratinocytes. RA was used for positive control. *#p<0.01* indicates a significant difference from the control. **p<0.05* and ***p<0.01* indicate a significant difference from the UVB-irradiated control. RA, retinoic acid;

Y. lipolytica oil potentially improve the skin conditions by inhibiting free radical production under oxidative stress (**Fig 5&6**).

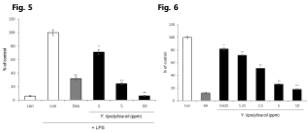


Fig 5. NO production by LPS treatment in HaCaT cells treated with different concentrations of *Y. lipolytica* oil. It was measured by NO detection kit. Dex was used for positive control.
**p<0.05* and ***p<0.01* indicate a significant difference from the LPS-treated control. Dex, dexamethasone;
Fig 6. The scavenging activity of free radical DPPH in HaCaT cells in the presence of *Y. lipolytica* oil. One mg per ml of ascorbic acid sample was used for positive control. **p<0.05* and ***p<0.01* indicates a significant difference from the control. AA, ascorbic acid;

Conclusions:

Oil extracted from extremophile *Yarrowia lipolytica* was in order to overcome the cold stress. In this study, cold stress induced by menthol treatment decreased expression levels of genes such as SOD2 and COL17. The oil extracted from *Y. lipolytica* increased expression level of these genes even in the menthol-induced keratinocytes. In addition, this oil alleviated the increase in MMP-1 expression and the decrease in procollagen synthesis by UVB irradiation in human keratinocytes. *Y. lipolytica* oil has a positive effect in skin anti-aging properties, suggesting that it would be a potent active cosmetic ingredient against a cold stress condition. Moreover, oxidative stress was diminished by *Y. lipolytica* oil in human keratinocytes. Fatty acids found in *Y. lipolytica* oil were similar to those of stratum corneum in human. It overall implied that *Y. lipolytica* oil can be able to use to improve skin condition both stress and normal condition.

Acknowledgements:

We thanked to professor Seo's Lab at Seoul National University to provide the oleaginous yeast Yarrowia lipolytica.

References:

1. Engebretsen, K. A., Johansen, J. D., Kezic, S., Linneberg, A., & Thyssen, J. P. (2016). Journal of the European Academy of Dermatology and Venereology, 30(2), 223-249.
2. Mäkinen, T. M., & Hassi, J. (2009). Industrial health, 47(3), 207-220.
3. Farage, M. A. (2008). Contact Dermatitis, 59(4), 226-232.
4. Wellmann, S., Bührer, C., Moderegger, E., Zelmer, A., Kirschner, R., Koehne, P., ... & Seeger, K. (2004). Journal of cell science, 117(9), 1785-1794.
5. Zhu, X., Bührer, C., & Wellmann, S. (2016). Cellular and molecular life sciences, 73(20), 3839-3859.
6. Caterina, M. J., & Pang, Z. (2016). Pharmaceuticals, 9(4), 77.
7. Schmidt, M. C., Askew, E. W., Roberts, D. E., Prior, R. L., Ensign Jr, W. Y., & Hesslink Jr, R. E. (2002). Wilderness & environmental medicine, 13(2), 94-105.
8. Martarelli, D., Cocchioni, M., Scuri, S., Spataro, A., & Pompei, P. (2011). The Journal of Sports Medicine and Physical Fitness, 51(2), 299-304.
9. Kim, J. T., Kang, S. G., Woo, J. H., Lee, J. H., Jeong, B. C., & Kim, S. J. (2007). Applied Microbiology and Biotechnology, 74(4), 820-828.
10. Abghari, A., & Chen, S. (2014). Frontiers in Energy Research, 2, 21.