

〈一般論文〉

琥珀アルコール抽出画分の皮膚ターンオーバー促進,
およびヒアルロン酸産生促進効果について

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**Effects of Ethanolic Amber Extracts on Epidermal Turnover
and Hyaluronic Acid Production**

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Abstract

In aged skin, delayed skin turnover and reduced production of hyaluronan are observed. Amber, fossil tree resins, has been used as ethnomedical since ancient times. We made ethanolic extracts from baltic amber, subjected them to a chromatography using a silicagel column chemically bonded to octadesyl silane, and eluted with methanol and hexane, and removed solvents to obtain five fractions according to the color of each eluate. Among these fractions, the fraction number 2 (6 $\mu\text{g}/\text{ml}$), a brown glutinous paste, increased mRNA expression of heparin-binding epidermal growth factor-like growth factor (HB-EGF) approximately 2-folds by cultured human keratinocytes, and increased its protein levels in an organotypic three-dimensional co-culture of human keratinocytes and dermal fibroblasts. Furthermore, topical applications of the fraction number 2 to mouse back skin resulted in accelerated disappearance of an ink stain made on mouse back skin, compared with the control skin treated with vehicle. And, the fraction number 2 (25 $\mu\text{g}/\text{ml}$) increased *hyaluronan synthase (HAS3)* mRNA level by approximately 4-folds and the amounts of hyaluronan in a human keratinocyte cell line, HaCaT cells. It increased HAS3 protein levels and altered the distribution of hyaluronan in organotypic three-dimensional co-cultures of epidermal keratinocytes and dermal fibroblasts. Furthermore, the amounts of hyaluronan were up-regulated around epidermal keratinocytes in mice following topical administration of the fraction number 2. In conclusion, two novel bioactivities of amber extracts were found. A fraction derived from ethanolic amber extracts was effective to induce *de novo* synthesis of HB-EGF and accelerate skin turnover. The amber extracts also promoted the production of hyaluronan, which may prevent dryness in the aged skin.

Key words: heparin-binding EGF-like growth factor (HB-EGF), hyaluronan, turnover, hyaluronic acid synthase, keratinocytes.