30PE-03

SUPPRESSING EFFECT OF ANTIOXIDANTS ON THE PHOTODEGRADATION OF TRANSDERMALLY APPLIED KETOPROFEN WITH UVA-EXPOSURE

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[Purpose] Topical ketoprofen (KP) is widely used for analgesic and anti-inflammatory. However, it has potential for photosensitization by the UV exposure resulting photoproducts of KP (KP-PPs) via radical reaction. The major KP-PPs are 3-ethylbenzophenone (Et-BP), 3-acetylbenzophenone (Ac-BP) and 3-(1-hydroxy)ethylbenzophenone (Et-BP-OH). In this study, suppressing effects of antioxidants, i.e., ascorbic acid (AA), 2-O-α-D-glucopyranosyl-L-ascorbic acid (AA-2G) and N-acetyl-cysteine (NAC), on the formation of 3 major KP-PPs in the skin in vivo were investigated.

[Method] 1) In vitro photodegradation: KP solution containing antioxidant was exposed to the UVA (approx. 0.23 J/cm²/min). 2) In vivo photodegradation: A piece of Mohrus® Tape (2.5 cm x 2.5 cm) (Hisamitsu Pharmaceutical Co.) was applied on the tape-stripped skin of the back of male Hartley guinea pig for 2 hr. Before and after the topical application of the Mohrus® Tape, aqueous antioxidant solution (75µL each) was applied (3 cm x 3 cm). After the removal of the Mohrus® Tape, the skin was irradiated with 10 J/cm² of UVA. One hour after the tape-removal, the skin was excised and extracted with chloroform. 3) Quantitative analysis: The amounts of KP and 3 major KP-PPs were determined by the HPLC equipped with a UV-detector.

[Result] Three antioxidants tested in this study showed significant suppressing effect in vitro. The in vivo formation of Et-BP was significantly suppressed by the treatment with AA and AA-2G. However, NAC did not suppress the Et-BP formation. The formation of the other 2 KP-PPs (Ac-BP, Et-BP-OH) was not significantly changed by the treatment with any antioxidants tested compared with the antioxidant-free control.

30PE-04

SUPEROXIDE SCAVENGING ACTIVITY OF PIRFENIDONE-IRON COMPLEX

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Pirfenidone (PFD) is focused on a new anti-fibrotic drug, which can minimize lung fibrosis etc. Recently, free radical is focused as the causative molecules in lung fibrosis. Therefore, we evaluated the superoxide (O2⁻) scavenging activities of PFD and the PFD–iron complex using electron spin resonance spectroscopy (ESR) with 5,5-dimethyl-1-pyrroline N-oxide (DMPO), luminol-dependent chemiluminescence assay, and cytochrome c reduction assay. As results, we confirmed that the PFD–iron complex was formed by mixing iron chloride with threefold molar PFD. The UV/vis spectrum of the PFD–iron complex was distinct from that of PFD or iron chloride. The strong binding ability of PFD and iron was confirmed by the competitive method with 1,10-phenanthroline. The PFD–iron complex reduced the amount of DMPO adduct produced for O2⁻ generated in the dose dependent manner of PFD-iron complex in the xanthine oxidase/hypoxanthine (XO/HX) system without inhibiting the enzyme activity by ESR spin trapping methods. PFD did not change the control signal, however, the PFD–iron complex significantly decreased in XO/HX system. The PFD–iron complex also reduced the amount of O2⁻ from phosphor ester-stimulated human neutrophils by ESR spin trapping methods. These inhibitory effects of the PFD–iron complex for O2⁻ was also confirmed by chemiluminescence and cytochrome c reduction assay. In conclusion, these results suggest the possibility that the O2⁻ scavenging effect of the PFD–iron complex contributes to the anti-fibrotic action of PFD used for treating idiopathic pulmonary fibrosis.