

# Investigation of an antioxidant containing ointment as therapeutic and preventive strategy for hand foot syndrome in cancer patients

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**Background:** Dermal side effects of chemotherapy such as the hand foot syndrome (HFS) can cause a major impairment in the quality of life of oncologic patients. Notably high incidences of up to 78% of HFS can be found in patients treated with pegylated liposomal doxorubicine, 5-fluorouracil, docetaxel and paclitaxel. The symptoms of HFS are classified into 3 severity grades, ranging from light erythema, edema and numbness to painful blisters, rhagades and erosions causing severe pain in affected patients. Up to now no preventive or therapeutic option has been found to effectively avoid HFS in order to continue chemotherapy. Hence, dose reduction or discontinuation of chemotherapy are frequent measures in HFS grade 3 patients. Here, radical formation after inverse penetration of chemotherapeutics in the skin as possible pathomechanism of HFS was shown and the effectiveness of a therapeutic and preventive strategy investigated based on these findings.

**Methods:** The visualization of the inside-out penetration of chemotherapeutics on the skin surface of patients treated with pegylated liposomal doxorubicin (PLD), 5-fluorouracil (5-FU), docetaxel (DT) and paclitaxel (PT) was investigated using laser scanning microscopy (LSM) in order to determine a possible local toxic effect.

Since such a toxic effect could likely be caused by radical formation, the carotenoid concentration of the skin was measured in these patients using resonance Raman spectroscopy. Measurements were conducted right before and after systemic application of chemotherapy in order to determine changes in the antioxidant status caused by radical formation.

Furthermore based on these previous investigations, a preventive strategy was designed using an antioxidant containing ointment applied in 17 patients receiving chemotherapy.

**Results:** It was shown that PLD was the only detectable chemotherapeutic on the skin surface by LSM after systemic application due to its fluorescent properties. A strong fluorescent signal was detected in the sweat glands, spreading over the skin surface.



The antioxidant status showed a decrease after application of all investigated chemotherapeutics. While 5-FU and PT showed only a moderate change in antioxidants, the most prominent decrease was found in PLD patients.

Since these findings suggested a local toxic effect of PLD in the skin, the preventive application of an ointment with a high radical protection factor was investigated in PLD patients and compared to a placebo ointment. Here, PLD showed a significant effect in the prevention of PLD-induced HFS grade 3 ( $p=0.003$ , Fisher's exact test), a lower overall incidence of PPE and significantly lower grades ( $p=0.026$ ) of HFS compared to placebo. Furthermore patients, who had developed a PPE grade 3 were immediately treated with the antioxidant ointment due to ethical reasons and showed an alleviation of skin symptoms so that chemotherapy could be continued as planned in these patients.

**Discussion:** An ointment with a high radical protection factor can be an effective preventive and therapeutic option for HFS accompanied by an important improvement of quality of life in affected patients. Further and larger studies will be necessary to confirm the effectiveness of this approach.