A CLINICAL SAFETY STUDY OF SALMON-ROE BIOLOGICAL ACTIVES DISSOLVED IN GLYCEROL MONOOLEATE SHOW NO IRRITATION OR SENSITIZATION ON HUMAN INTACT AND WOUNDED SKIN

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Introduction: Salmon roe extracts have shown the ability to accelerate 2-degree burn wounds in human explant skin (C. Clemm et al. European Tissue Repair Society-Wound Healing Society, 2015, Wound Rep Reg (2015) 23 A1–A37). Several vehicles for topical administration of salmon roe extracts have been explored by us and here we report that a glycerol- mono and dioleate mixture (55/30% w/v GMO/DMO) with 12% (w/v) salmon roe extract creates an optimal polar lipid carrier for dispersion of roe extract dissolves roe extract and provides a polarlipid matrix that stabilizes proteins in the formulation.GMO forms various liquid crystalline phases in the presence of different amounts of water. In the presence of a small amount of water, GMO forms reversed micelles characterized by an oily texture. As more water is added, a soft gel system is formed that corresponds to the lamellar phase. In addition, the temperature and ratio of weight to water plays a role in the various phases of GMO.GMO is regarded as a permeation enhancer due to its amphiphilic property. It is considered as a nontoxic, biodegradable, and biocompatible material classified as "generally recognized as safe" (GRAS). It is included in the FDA Inactive Ingredients Guide and present in nonparenteral medicines in the United Kingdom (A Ganem-Quintanara et al., Drug Development and Industrial Pharmacy, Volume 26, Issue 8, 2000). A combination of GMO and Vernex 12% (w/v) was selected for further assessment of skin safety in both intact and breached skin.

Methods: The study was an open, unblinded, study, designed to assess skin irritation and sensitization of topical 12% (w/v)salmon roe extract (Vernex) dissolved in 60% glycerol monololeate (GMO) o.d. over 5 days. Both non-allergic subjects and subjects with mild topical allergy were included. Sensitization was assessed by prick testing and IgE measurements in a small sub cohort exposed to 100% (w/v) o.d. to 2 degree burn/suction wounds over 4 weeks prior by topical exposure of 5 days as the main cohort.

Results: In the cohort of 20 human volunteers, exposed to 5 days repeated dosing of a purified salmon roe extract (Vernex) in GMO on the volar surface of the left underarm, no adverse reactions to the treatment was observed. 3 subjects were exposed to 100% concentrated salmon roe extract applied directly to secondary burn/suction wounds for time period over 4 weeks, which was followed by 5 days topical exposure with GMO/Vernex. No IgE increase or prick test reactions indicative of sensitization to salmon roe or GMO was observed. The wounds healed rapidly with no scarring.

Conclusion: GMO with Vernex 12% (v/w) did not cause irritation or sensitization in a small cohort of healthy volunteers and showed favorable properties as a topical carrier for protein bio actives, enhacing stability and possibly also skin permability. On human skin, probably due small amounts of water uptake from skin along with the elevated temperature of the skin in comparison to the storage one (room temperature), GMO apparently formed a reversed micellar oily texture (within seconds) upon administration.

Acknowledgments: This research was supported by grants from the EU commissionEurostars (9477 OCWHD VERNEX), Vinnova, Sweden and from Norwegian Research Council