

Competence Centre skintegral™

Integrative research on natural compounds, dermatopharmacy and photodermatology

Head

Prof. Dr. med. Dipl. Biol. Christoph M. Schempp

Team

- Cornelia Martin (Office)
- Dr. rer. nat. Ute Wölfle, Ph.D.
- Dr. med. Federica Casetti
- Birgit Haarhaus, B.T.A.
- Beatrix Starke (study nurse)
- Julia Hoffmann (doctoral candidate)

Contact

Competence Centre skintegral™

Phone	+49-761-270 67830
Fax	+49-761-270 67831
E-Mail	skintegral@uniklinik-freiburg.de
Internet	www.skintegral.de

Aims

The competence centre skintegral™ at the department of dermatology is dedicated to the investigation of beneficial effects of plant extracts on the skin. Secondary plant metabolites and standardized plant extracts contain a variety of natural compounds with therapeutic relevance, such as free radical scavenging, antiinflammatory and antimicrobial substances. The dermatologic usability of most of these compounds is only partly explored. The efficacy and skin tolerability of natural compounds in topical preparations depends on the liberation and penetration of the compounds from the vehicle, a scientific field covered by dermatopharmacy. Natural compounds used in dermatology should not display toxic, skin sensitizing or phototoxic properties. The compounds are screened in cell culture and enzyme inhibition assays for toxic effects. Subsequently their tolerability and effectivity is assessed in vivo using patch tests or the ultraviolet erythema test (photodermatology). Where appropriate, plant extracts, compounds or procedures that have proven beneficial in pilot studies are patent protected, and licensed to industrial partners for product development. The competence centre skintegral™ is integrated into the clinical divisions of the department of dermatology. It performs its tasks in cooperation with the other institutions of the University Medical Center Freiburg, allowing for close connection to clinical research. The integrative approach of skintegral™ is expressed by interdisciplinary research projects with natural sciences such as allergology, pharmacy and biology, as well as complementary research and therapies.

Scientific projects

Prevention of ultraviolet-mediated and toxic skin damage by flavonoids

Flavonoids are secondary plant polyphenols with a very high antioxidant capacity that are able to neutralize skin damaging reactive oxygen species. The plant *Reseda luteola* (weld) that is growing on wasteland and fallows contains high amounts of the flavonoid luteolin. It is a polyphenol with a long history: the Romans were cultivating *Reseda luteola* and were dyeing their clothes in yellow with luteolin. The competence centre skintegral™ currently cooperates as academic partner with the pharmaceutical company BRECHT GmbH in the development of a skin protective product series. It is based on a patent protected flavonoid extract from *Reseda luteola*, and it is designed for commercial skin protection in the industrial field, and for the aged skin, too. This work is supported by a grant from the German Federal Ministry of Economics and Technology (grant no. KF2556501SK0).

Tannins in the treatment of skin inflammation and histamin-mediated reactions

Tannins represent another group of plant polyphenols with prominent antioxidative properties. Moreover, tannins chemically react with proteins and have therefore been used for the tanning of leather. In the molecular range tannins are highly effective immune modulators and anticancer agents. Today, plant derived tannins are mainly used in anthroposophic medicine as therapeutics that regulate increased cell proliferation, edema and atopic diseases. Tannin containing drugs are generated from oak bark and from tormentil, for example. The competence centre skintegral™ cooperates with the pharmaceutical company WALA that produces several tannin containing anthroposophic drugs in performing plant studies, clinical and experimental research on tannin containing plants.

Use of antimicrobial plant extracts for the prevention and treatment of bacterial skin infections

Many skin disorders are caused by (impetigo, acne, rosacea) or aggravated by (acute eczema, atopic dermatitis) bacterial colonization of the skin. Therefore, there is a continued demand for topical compounds with antiseptic or antibiotic activity. However, topical antibiotics are obsolete because of the risk of inducing resistance of bacteria against topical antibiotics. Therefore, the competence centre skintegral™ cooperates since many years with the group of Professor Uwe Frank at the

[institute of environmental medicine and hospital](#)

to explore and develop new plant extracts with antiseptic properties. Some proof of concept studies have been performed, and the competence centre skintegral™ is also involved in patent applications on the use of St. John's wort (hyperforin), *Usnea barbata* (usnic acid) and coriander oil for the treatment of skin infections. At the present a clinical trial investigates the effect of a plant-based skin care series for impure skin.

Clinical and molecular interactions of betulines and the skin

The competence centre skintegral™ has been involved in clinical and experimental research on betulines and the skin. It has conducted non interventional studies that have shown that topical betulin is effective in the treatment of skin conditions with an impaired skin barrier (intertrigo, burns, acute eczema, superficial wounds). Additionally, the competence centre skintegral™ has shown an efficacy of betulin-based emulsions in the treatment of actinic keratoses (AK) in proof of concept studies. In the present the competence centre skintegral™ participates in a multinational multicentric placebo-controlled study (BETAtrial) that evaluates the efficacy of betulin-based oleogel in AK. The competence centre skintegral™ also contributed to the

[first betulin symposium](#)

of the betulin institute in february 2010.

Services

The competence centre skintegral® provides various services in the context of contracted research. These include primarily physiological investigations with regard to skin hydration levels, transepidermal waterloss, cutaneous circulation and skin pigmentation. Patchtesting is also undertaken. Integrated into the competence centre is a study centre for inflammatory dermatoses which comprises a study nurse and doctors certified in the running of clinical studies according to good clinical practice.

Selected papers

- Strüh CM, Jäger S, Schempp CM, Scheffler A, Martin SF (2011) A novel triterpene extract from mistletoe inhibits cell growth and induces rapid apoptosis in murine B16.F6 melanoma cells. *Phytother Res* (accepted)
- Leuner K, Kraus M, Woelfle U, Beschmann H, Harteneck C, Boehncke WH, Schempp CM, Müller WE (2011) Reduced TRPC channel expression in psoriatic keratinocytes is associated with impaired differentiation and enhanced proliferation. *PLoS ONE* 6(2):e14716. doi:10.1371/journal.pone.0014716
- Casetti F, Bartelke S, Biehler K, Augustin M, Schempp CM, Frank U (2011) Antimicrobial activity against bacteria with dermatological relevance and skin tolerance of the essential oil from *Coriandrum sativum* L. fruits. *Phytother Res* 25: 2011 Aug 4. doi: 10.1002/ptr.3571.

- Wölfle U, Esser PR, Simon-Haarhaus B, Martin SFM, Lademann J, Schempp CM (2011) UVB-induced DNA damage, generation of reactive oxygen species and inflammation is effectively attenuated by the flavonoid luteolin in vitro and in vivo. *Free Rad Biol Med* 50:1081-1093
- Casetti F, Wölfle U, Gehring W, Schempp CM (2011) Dermocosmetics for dry skin - a new role for botanical extracts. *Skin Pharmacol Physiol* 25:289-293.
- Casetti F, Miese A, Mueller ML, Simon JC, Schempp CM (2011) Double trouble from sunburn: UVB-induced erythema is associated with a transient decrease of skin pigmentation. *Skin Pharmacol Physiol* 24:160-165
- Huber R, Bross F, Schempp C, Gründemann C (2011) Arnica and stinging nettle for treating burns - A self-experiment. *Compl Ther Med* 19:276-280.
- Wölfle U, Laszczyk MN, Kraus M, Leuner K, Kersten A, Simon-Haarhaus B, Scheffler A, Martin SF, Müller WE, Nashan D, Schempp CM (2010) Triterpenes promote keratinocyte differentiation in vitro, ex vivo and in vivo. A role for the transient receptor potential canonical 6. *J Invest Dermatol* 130:113-23
- Wölfle U, Simon-Haarhaus B, Mefort I, Schempp CM (2010) Reseda luteola L. extract displays anti-proliferative and pro-apoptotic activities that are related to its major flavonoids. *Phytotherapy Res* 24:1033-1036
- Weckesser S, Laszczyk MN, Müller ML, Schempp CM, Schumann H (2010) Topical treatment of necrotising herpes zoster with a betulin-based emulsion obtained from birch bark. *Res Compl Med* 17:271-273
- Reuter J, Wölfle U, Weckesser S, Schempp CM (2010) Which plant for which skin disease? Part 1: Atopic dermatitis, psoriasis, acne, condyloma and herpes simplex. *JDDG* 8:788-796
- Reuter J, Wölfle U, Korting HC, Schempp CM (2010) Which plant for which skin disease? Part 2: Dermatophytes, chronic venous insufficiency, photoprotection, actinic keratoses, vitiligo, hair loss, cosmetic indications. *JDDG* 8:866-874
- Wölfle M, Martin SF, Emde M, Schempp CM (2009) Dermatology in the Darwin anniversary 2: evolution of the skin associated skin immune system. *JDDG* 7: 862-869
- Schempp CM, Emde M, Wölfle U (2009) Dermatology in the Darwin anniversary 1: the evolution of the skin. *JDDG* 7:750-757
- Jocher A, Nist G, Weiss J, Wetzel D, Merfort I, Jakob T, Schempp CM (2009) Allergenic potential of Arnica-containing formulations in Arnica-allergic subjects. *Contact Dermatitis* 61:304-306
- Casetti F, Jung W, Wölfle U, Reuter J, Neumann K, Gilb B, Wähling A, Wagner S, Merfort I, Schempp CM (2009) Topical application of solubilized Reseda luteola extract reduces ultraviolet B-induced inflammation in vivo. *J Photochem Photobiol (B)* 96:260-265
- Huyke C, Reuter J, Rödiger M, Kersten A, Laszczyk M, Scheffler A, Nashan D, Schempp CM (2009) Treatment of actinic keratoses with a novel betulin-based oleogel. A prospective, randomized, comparative pilot study. *JDDG* 7:128-134
- Müller M, Hill K, Beschmann K, Rubant S, Boehncke WH, Harteneck C, Schempp CM, Müller WE, Leuner K (2008) Specific TRPC6 channel activation, a novel approach to stimulate keratinocyte differentiation. *J Biol Chem* 283:33942-54
- Reuter J, Huyke C, Scheuven H, Ploch M, Neumann K, Jakob T, Schempp CM (2008) Skin tolerance of a new bath oil containing St. John`s wort extract. *Skin Pharmacol Physiol* 21:306-311
- Reuter J, Huyke C, Casetti F, Theek C, Frank U, Augustin M, Schempp CM (2008) Anti-inflammatory potential of a lipolotion containing coriander oil in the ultraviolet erythema test. *JDDG* 6:847-851
- Reuter J, Jocher A, Stump J, Franke G, Grossjohann B, Schempp CM (2008) Investigation of the anti-inflammatory potential of Aloe vera gel (97.5%) in the ultraviolet erythema test. *Skin Pharmacol Physiol* 21:106-110
- Lass C, Vocanson M, Wagner S, Schempp CM, Nicolas JF, Merfort I, Martin SF (2008) Anti-inflammatory and immune regulatory mechanisms prevent CD8+ T cell-mediated contact hypersensitivity to Arnica montana L. in immunocompetent mice. *Exp Dermatol* 17:849-857
- Engel K, Reuter J, Seiler C, Schulte Mönning J, Jakob T, Schempp CM (2008) Anti-inflammatory effect of pimecrolimus in the sodium lauryl sulphate test. *JEADV* 22:447-450
- Engel K, Schmidt U, Simon-Haarhaus U, Schempp CM (2007) Usnea barbata extract prevents ultraviolet-B induced prostaglandin E2 synthesis and COX-2 activation in HaCaT keratinocytes. *J Photochem Photobiol (B)* 89:9-14
- Reuter J, Jocher A, Hornstein S, Schulte Mönning J, Schempp CM (2007) Sage extract rich in phenolic diterpenes inhibits ultraviolet-induced erythema in vivo. *Planta Med* 73:1190-1191
- Huyke C, Simon-Haarhaus B, Quirin KW, Schempp CM (2007) Composition and biological activity of different extracts from Schisandra sphenanthera and Schisandra chinensis. *Planta Med* 73:1116-1126
- Weckesser S, Engel K, Wittmer A, Pelz K, Schempp CM (2007) Screening of plant extracts for antimicrobial activity against bacteria and yeasts with dermatological relevance. *Phytomedicine* 14:508-516
- Stancu E, Braun-Falco M, Bruckner-Tuderman L, Schempp CM (2007) Umbilicated blisters on sun-exposed skin. *Hautarzt* 58:343-346.
- Laszczyk M, Jäger S, Simon-Haarhaus B, Scheffler A, Schempp CM (2006) Physical, chemical and pharmacological characterization of a new oleogel forming triterpene extract from the outer bark of birch (Betulae cortex). *Planta Med* 72:1389-1395
- Hrenn A, Steinbrecher T, Labahn A, Schwager J, Schempp CM, Merfort I (2006) Plant phenolics inhibit neutrophil elastase and proliferation of keratinocytes. *Planta Med* 72:1127-1131
- Sammain A, Jocher A, Bruckner-Tuderman L, Schempp CM (2006) Lupus vulgaris--a case diagnosed more than 20 years after onset. *JDDG* 4:958-960.
- Schempp CM, Simon-Haarhaus B, Krieger R, Simon JC (2006) Solar simulator induced phototoxicity of the furoquinoline alkaloid dictamnine compared to 8-methoxypsoralen and 5-methoxypsoralen. *Planta Med* 72:941-943