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JID

JOURNAL OF INVESTIGATIVE DERMATOLOGY



The banner features a light blue background with a molecular structure on the left and a circular inset on the right. The inset shows a woman in a white lab coat working at a desk with a laptop and a microscope. The SID logo is in the top right corner of the inset.

2020
SID Annual Meeting
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MAY 13-16, 2020

Society for Investigative Dermatology 2020

Society for Investigative Dermatology 2020

May 13–16, 2020

SID Virtual Conference

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* Category Name Amended (February 2020)

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Formulation and evaluation of topical products with *Helianthus Annuus* ozonized oilM Andreassi, C Salvini, L Furi, J Zanardi, P Brizzi and V Travagli *Department of Biotechnology, Chemistry and Pharmacy, University of Siena, Siena, Italy*

This work was aimed to study the activity of topical products formulated with *Helianthus annuus* normal and ozonized oil produced in Italy. Recent studies have suggested a possible moisturizing and elasticizing activity of *Helianthus Annuus* ozonized oil. For such characteristics *Helianthus Annuus* ozonized oil appears an appropriate ingredient to be used in topical preparations for the treatment of skin hydration. The oil was incorporated into O/W emulsion in a standard formulation at percent concentration of 3%, 5% and 10 % respectively of *Helianthus Annuus* normal and ozonized oil, one O/W emulsion was prepared without active ingredient as control. The investigation was carried out on 10 healthy female volunteers, between the ages of 20 and 40, with normal or dry skin. Each product was applied to the volar surface of the forearm at a dose of 3 mg/cm². As control, the same cream without active ingredient was applied to the other forearm. To evaluate TEWL and skin elasticity, was used the device Aveal 220 (Sylton diagnostic systems). The skin hydration action of the emulsions was evaluated in relation to basal value, and the emulsion without active ingredient, respectively after 15 minutes and 8 days. The skin elasticity was evaluated after 15 minutes and 8 days. The results showed that the 6 emulsions with *Helianthus Annuus* normal and ozonized oil, compared to the emulsion without active, significantly increase the degree of hydration and elasticity of the skin. The 10% formulation of *Helianthus Annuus* ozonized oil has a greater power of hydration of the skin compared to other emulsions, both short and long term and is the emulsion that has produced better results.



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Saikosaponin A induces HEKa cell apoptosis via ROS generationM Liu and Y Zheng *Dermatology, the Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, China*

Background: Psoriasis is a common, chronic and noninfectious skin disease with the complex pathogenesis which is reported as excessive proliferation and aberrant apoptosis of keratinocytes. Saikosaponin A (SSA) is a kind of triterpenoid saponin extracted from Chinese traditional medicine *Radix bupleuri*, possessing various biological functions such as anti-inflammatory, immune regulation and anti-tumor. But the effect of SSA on keratinocytes is unclear. **Objective:** To explore the effect of SSA on keratinocytes and to analyze the corresponding mechanism. **Methods:** 1. The cell viability was detected by MTT assay and the apoptosis was examined using the annexin V-FITC/PI flow cytometry double staining method. Apoptosis-related protein were determined by Western blot. 2. After stimulation with SSA, DCFH-DA and JC-1 were used to detect intracellular reactive oxygen species (ROS) levels and mitochondrial membrane potential. MitoSOX Red and MitoTracker Green were used to observe generation and distribution of ROS in mitochondria by confocal laser scanning microscope; ROS-related protein was detected by Western blot. 3. Antioxidants N-acetylcysteine (NAC, 10mM) was added to HEKa cells 1h before SSA(20μM) treatment to identify whether SSA induced the apoptosis of HEKa cells through ROS production. **Results:** 1. Compared with the control group, SSA significantly inhibited the viability and induced the apoptosis of HEKa cells with changes in BCL-2 family protein levels. 2. SSA promoted ROS production of mitochondria and decreased Δψ, which caused changes in ROS-related protein levels and oxidative stress damage to cells. 3. SSA-treated HEKa cells produced more ROS, but this effect was inhibited by the antioxidants NAC. Furthermore, NAC treatment attenuated HEKa cell apoptosis and proliferation suppression of SSA. **Conclusion:** SSA can inhibit proliferation and induce apoptosis of HEKa cells through ROS generation, making SSA a potential promising candidate drug for future research.



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Development and first-in-human characterization of a potent oral CCR4 antagonist for the treatment of atopic dermatitisLE Cheng, A Jorapur, S Jacobson, O Talay, S Miakicheva, D Trujillo, N Lee, J Jankicevic, DWustrow, P Kassner, W Ho and D Brockstedt *RAPT Therapeutics, Inc., South San Francisco, California, United States*

Atopic dermatitis (AD) is predominantly driven by T helper type 2 cells (Th2). Accumulation of Th2 cells depends on CCR4-mediated recruitment of Th2 cells by the CCR4 ligands CCL17 and CCL22. Both are elevated in inflamed tissue, and levels correlate with disease activity and severity. Here, we describe RPT193, a novel, highly potent and specific oral CCR4 antagonist. In multiple preclinical mouse models of allergic skin inflammation, we demonstrated efficacy and reduction of Th2 cytokines with once daily dosing of RPT193 that is comparable to antibodies specific to IL-4 receptor and IL-13. The safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of escalating single and multiple oral (once daily for 7 days) doses of RPT193 are currently being evaluated in healthy adults. The study has enrolled healthy subjects into 4 single and 4 multiple dose cohorts (randomized 3:1 to receive RPT193 ranging from 50-400 mg or placebo). As of an ad hoc interim analysis, 64 healthy subjects have received single or multiple doses of RPT193 or placebo. Blinded safety review suggests RPT193 has acceptable safety and tolerability with only mild or moderate treatment-emergent adverse events after single or multiple doses. No stopping criteria were met at any dose tested. RPT193 demonstrated linear PK, a terminal half-life of ~24 hours, and accumulation upon multiple dosing. CCR4 receptor occupancy of >80% at 24 hours post-dose was attained in most subjects receiving single doses and all subjects receiving multiple doses of RPT193. In summary, preclinical data indicate that CCR4 antagonism with RPT193 inhibits allergic skin inflammation in mice akin to targeting IL-13 or the IL-4 receptor. Clinical experience thus far indicates encouraging safety, PK consistent with once daily dosing, and desired target coverage. The data warrant further investigation of RPT193 in patients with AD and potentially other allergic immune conditions.



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Biological evaluation of litchi derived products as dermatological agentsD Huang¹, Z Sun¹, X Shen¹, Q Cu¹, M Soeberdt², C Abels² and J Xu¹ *1 School of Pharmaceutical Sciences, Sun Yat-Sen University, Guangzhou, Guangdong, China and 2 Dr August Wolff, Bielefeld, Germany*

Litchi (*Litchi chinensis* Sonn.) is a fruit native to South China, and popular for the taste and health benefits. Litchi products, such as litchi juice and vinegar (extracted or fermented from litchi fruit) have potential dermatological benefits. In this paper, we have evaluated litchi vinegar and juice regarding protective effects on HaCaT keratinocytes following either UVB irradiation or poly (I:C) by assessing cell survival (OD, optical density; MTT assay), reactive oxygen species (ROS), superoxide dismutase (SOD), and glutathione peroxidase (GSH-Px) activity. In addition, different inflammatory parameters were measured, e.g. IL-1b, TNF-α, or IL-8. As result litchi vinegar or juice (1) are not cytotoxic at therapeutic concentration; (2) protect HaCaT keratinocytes against UVB irradiation or poly(I:C); (3) reduces oxidative stress through inhibiting ROS and enhancing SOD and GSH Px activity; (4) suppressing inflammatory parameters, e.g. IL-1b, TNF-α, and IL-8. The ingredients very likely responsible for these effects are primarily epicatechin, rutin and chlorogenic acid.



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ATx201 modulates biomarkers of skin barrier function and cutaneous inflammation in patients with moderate atopic dermatitisE Guttman-Yassky¹, R Bissonnette², A Pavel¹, E Saint-Cyr Proulx², P Prokocimer³, R Toft-Kehler³ and M Sommer³ *1 Icahn School of Medicine at Mount Sinai, New York, New York, United States, 2 Innovaderm Research, Montreal, Quebec, Canada and 3 UNION Therapeutics, Hellerup, Denmark*

ATx201 is a small molecule, which decolonizes *Staphylococcus aureus* and improves the diversity of the skin microbiome in patients with mild-to-severe atopic dermatitis (AD) (DECOLAD). We now report the safety and immune-modulatory effect of ATx201 in patients with moderate AD. In this randomized, double-blind, intraindividual, and vehicle-controlled Phase 2 trial, thirty-one patients received ATx201 CREAM 2% and matching vehicle (1:1) once daily for 3 weeks (NCT03304470), with a 12-day follow-up period. Analysis of the safety data revealed that ATx201 CREAM 2% was generally safe and well-tolerated in subjects with moderate AD lesions. The histological and transcriptional profiling analysis (IHC, microarray and RT-PCR) demonstrated that treatment with ATx201 CREAM 2% significantly ($p < 0.05$) increased expression of biomarkers related to skin barrier function (PNPLA3, ACOX2, DGAT2, FAXDC2, etc.), and decreases expression levels of markers related to inflammation including Th17 (S100A7, S100A9, CCL20, PI3, CXCL1, IL17C, STAT3), Th2 (IL10, IL4R, CCL26, CCL18, etc.), Th1 (CCL2, CCR1, etc.) and inflammatory cells (Langerin/CD207) compared to vehicle at Day 22. Finally, several biomarkers that were significantly modulated by ATx201 CREAM 2% were significantly correlated with improvement in TSS, TAA scores and the TSS component scores ($p < 0.05$), such as S100A8 ($p_{TSS} = 0.83$), KRT16 ($p_{TSS} = 0.77$), PI3 ($p_{TSS} = 0.69$), IL13 ($p_{TSS} = 0.68$), IL22 ($p_{TSS} = 0.67$) and MMP12 ($p_{TSS} = 0.55$). IHC analysis further revealed that 15/29 (51.7%) subjects were classified as histological responders receiving ATx201 CREAM 2% versus 9/29 (31.0%) receiving vehicle. These data suggest that topical application of ATx201 is safe and improves biomarkers of skin barrier function and suppresses biomarkers of AD-associated inflammation across multiple T helper cell pathways.



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Preclinical rationale for a first-in-human trial to evaluate the safety and preliminary efficacy of desmoglein 3 chimeric autoantibody receptor T cells (DSG3-CAART) for mucosal pemphigus vulgarisAS Payne, J Lee, DK Lundgren, X Mao, S Manfredo-Vieira, S Nunez-Cruz, EF Williams, C Assenmacher, E Radaelli, B Wang, CT Ellebrecht, JA Fraietta and MC Milone *University of Pennsylvania, Philadelphia, Pennsylvania, United States*

We previously established proof-of-concept that antigen-specific B cell depletion can be achieved with gene-engineered T cells expressing chimeric autoantibody receptors (CAARs) comprising DSG3, the autoantigen in the autoimmune blistering disease mucosal pemphigus vulgaris (PV), fused to CD137-CD3ζ signaling domains. After specific lysis of anti-DSG3 B cells, DSG3-CAART cells are stimulated to proliferate and engraft, leading to potentially durable remissions of autoimmune disease. Here we present final preclinical studies supporting the DSG3-CAART investigational new drug application. DSG3-CAART specifically lysed primary human anti-DSG3 B-cells from PV patients and demonstrated dose-related activity in a PV hybridoma model, resulting in decreased hybridoma burden, decreased serum and tissue-bound autoantibodies, and increased DSG3-CAART engraftment. In an exploratory PV active immune model with physiologic anti-DSG3 IgG levels, DSG3-CAART inhibited antibody responses against pathogenic DSG3 epitopes and autoantibody binding to epithelial tissues, leading to clinical and histologic resolution of blisters. Soluble anti-DSG3 antibody stimulates DSG3-CAART cells to promote IFNγ secretion, homotypic clustering, and clonal proliferation, consistent with an activated T cell phenotype. In vitro screening of a panel of primary human cells with DSG3-CAART and high-throughput screening of a commercial membrane protein array with the soluble DSG3 CAAR ectodomain did not identify productive interactions with desmosomal or other off-target proteins. Collectively, these studies have informed the clinical design of a first-in-human trial of DSG3-CAART for mucosal PV and may facilitate the preclinical development of future CAART therapies for other antibody-mediated diseases.



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