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## Peru Balsam & Propolis Bibliographies.

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– “Positive reactions to balsam of Peru in propolis-sensitive individuals are explicable because many compounds are common to both materials” – Hausen (1988).

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### Peru Balsam.

#### **Beneficial Effects & Uses.**

Anon (1986): Monograph *Balsamum peruvianum*, *Bundesanzeiger* No **173** Sept 18, 1986.

Anon(1913) “Therapeutic value of balsam of Peru.” *The Lancet* **181**, 4666, 335-6.

Arctander S. (1960) *Perfume & Flavour Materials of Natural Origin* Elizabeth N.J.: published by the author pp 521, 523.

de Barros Machado T, Leal I.C., Kuster R.M., Amaral A.C., Kokis V., de Silva M.G. & dos Santos K.R. (2005). "Brazilian phytopharmaceuticals--evaluation against hospital bacteria." *Phytother Res.* **19**(6), 519-25. [Abstract](#). Pharmaceutical companies have demonstrated renewed interest in investigating higher plants as sources for new lead structures and also for the development of standardized phytotherapeutic agents of proven efficacy, safety and quality. This work analysed three commercial phytopharmaceuticals against multi-resistant bacteria of medical importance, including methicillin-resistant *Staphylococcus aureus* isolates from the Brazilian endemic clone.

From the phytopharmaceuticals assayed, plants from the products 'Astmo-flora' and 'Kókolos' were considered active, while plants from 'Uva do Mato' were not active in the tested concentrations, which ranged from 62.5 to 500 microg/mL. Among fractions of *Aristolochia cymbifera* and *Myroxylon balsamum*, the hexane extracts showed the best results against *Staphylococcus* spp. and *Pseudomonas aeruginosa*. These fractions showed growth inhibition of all methicillin-sensitive and -resistant *Staphylococcus aureus* strains and the majority of the *Pseudomonas aeruginosa* strains at a concentration of 500 microg/mL. Bioassay-guided fractionation of hexane extracts of *Aristolochia cymbifera* and *Myroxylon balsamum* led to the identification of the diterpene 2-oxo-populifolic acid and of the chalcone isoliquiritigenin, respectively, as antimicrobial compounds.

Beitz J.M. (2005) "Heparin-induced thrombocytopenia syndrome bullous lesions treated with trypsin-balsam of peru-castor oil ointment: a case study." *Ostomy Wound Manage.* **51**(6), 52-4, 56-8. [Abstract](#). Heparin-induced thrombocytopenia syndrome is a serious, potentially life-threatening adverse reaction to the use of heparin anticoagulation therapy that can result in significant skin damage and organ morbidity. A case study design is used to describe the innovative use of a topical wound treatment (trypsin-balsam of Peru-castor oil ointment) on bullous lesions related to the effects of this syndrome. An elderly, morbidly obese woman was treated for 2 weeks with twice-daily applications of the product along with non-adherent oil emulsion dressings. Oozing decreased substantially within a few days and open blisters closed within 1 week. After 2 weeks of therapy, the bullous skin reaction was fully resolved with no recurrence. The results of this case study suggest that this topical product may have had a positive effect on the bullous lesions and should be considered for use in other similar significant integumentary reactions.

Bergemann J. (1950) "3 Mitteilung: Der Perubalsam; Handelsnamen, Geschichte, Gewinnung und Produktion." *Pharmazie* **5**, 450-455.

Billot M. & Wells F.V. (1975) *Perfumery Technology* Ellis Horwood Chichester p 114.

Bohacek L. & Farley K. (undated) "Improved Healthcare Outcomes in Partial Thickness Wounds" - see <http://www.healthpoint.com/divisions/tm/Bohacekpaper.pdf>

Carson S.N., Wiggins C., Overall K. & Herbert J. (2003) "Using a castor oil-balsam of Peru-trypsin ointment to assist in healing skin graft donor sites." *Ostomy Wound Manage.* **49**(6), 60-4. [Abstract](#). Skin graft donor sites are partial-thickness wounds that are commonly managed with gauze-type dressings. As such, they often cause more pain and difficulty in healing than the graft-recipient site. A retrospective study was conducted to ascertain the effects of using a castor oil-balsam of Peru-trypsin containing ointment on skin graft donor sites in 36 consecutive patients (16 female, 20 male). All donor sites were epithelialized after 11 days (range 6 to 11 days, mean 8 days) and no wound complications were observed. Given these healing results and product ease of use, this particular formulation has become the facilities' current treatment of choice and further study is indicated and warranted.

Kastrup E.K., Olin B.R., Connell S.I., & Hebel S.K. (eds) (1989) "Facts and Comparisons" *St. Louis MO, Facts and Comparisons*, 1989

Fastvedt E., Stashak T.S., & Othic A. (2004) "Update on Topical Wound Medications" *Clinical Techniques in Equine Pract.* **3**(2), 164-172. [Abstract](#). Numerous topical wound medicants are available today. Very few of these products have been tested in the horse. Due to the unique nature of wound healing in the distal limbs of horses (carpus, tarsus and distad), many beneficial effects of these medicants seen in other species and in vitro have not been reproduced in equine limb wounds. There is an abundance of literature regarding topical wound medicants; however, the findings of these studies are quite variable, in general. Many wound care articles have questioned the routine use of topical medications, preferring the concept of moist wound healing in which the body produces all the substrates necessary for adequate wound healing. This article outlines many of the common products that are available to equine practitioners and provides

current information regarding their use in wound healing. Unfortunately no product or substrate has been shown to be superior for equine wound management. That being said, the information provided in this article will attempt to provide the practitioner with information necessary to make educated decisions regarding the selection of topical medicants for wound care.

Gallant A.E. (1897) "Report on the use of a mixture of castor oil and Peru balsam as a surgical dressing." *Annals of Surgery* **26**(3), 329-339.

Glenn J. (2006) "Managing a traumatic wound in a geriatric patient." *Ostomy Wound Management* **52**(4), 94-8. [Abstract](#). Clinical management of a wound in a geriatric patient requires an understanding of age-related changes in the skin and the knowledge to make appropriate treatment choices. This case study describes clinical assessment and management of a traumatic hip wound in a 75-year-old patient. In addition to addressing his nutritional status by providing supplements, topical wound care preparations, including papain-urea and castor oil/balsam of Peru/trypsin, were used as a conservative approach to address debridement and periwound skin concerns. Extra vigilance is required to assess wounds in geriatric patients to determine proper wound treatment and achieve optimum results. Additional studies to evaluate optimal treatment strategies in the clinical management of traumatic wounds in the geriatric population are needed.

Gray M. (2004) "Preventing and managing perineal dermatitis: a shared goal for wound and continence care." *J. Wound Ostomy Continence Nurs.* **31**(Suppl 1), 2-9; quiz S10-2.

Gray M. & Jones D.P. (2004) "The effect of different formulations of equivalent active ingredients on the performance of two topical wound treatment products." *Ostomy Wound Manage.* **50**(3), 34-8, 40, 42-4. [Abstract](#). Product selection for the management of pressure ulcers or perineal dermatitis is typically based on consideration of active ingredients, but a growing body of evidence suggests that delivery vehicles also may influence product safety and efficacy. A 10-day, randomized, controlled experimental study was conducted to compare the safety and efficacy of two prescription products used for the treatment of pressure ulcers and perineal dermatitis. Both products contain equivalent active ingredients (balsam of Peru, castor oil, and trypsin), but one product delivers these ingredients in an ointment base while the other uses an aerosol spray. Sixty healthy volunteers (> 65 years of age) underwent intentional creation of two equivalent skin wounds (approximately 6 mm in diameter) using an Erbium-YAG laser. Volunteers served as their own control. Wounds were randomized to treatment with one of the balsam of Peru products or saline. Wounds were evaluated every other day. Significant differences between treatments were observed for most outcome variables (edema, scabbing, erythema, epithelialization). Wounds managed with the ointment-based product had lower edema, scabbing, and erythema scores and higher epithelialization scores than the spray or saline managed wounds. The results of this study confirm that formulation of the vehicle base can have a significant effect on product safety and effectiveness.

Ohsaki, A., Takashima J., Chiba N. & Kawamura M. (1999). "Microanalysis of a selective potent anti-*Helicobacter pylori* compound in a Brazilian medicinal plant, *Myroxylon peruiferum* and the activity of analogues. *Bioorg. Med. Chem. Lett.* **9**(8), 1109-12. [Abstract](#). A selective potent anti-*Helicobacter pylori* isoflavone was isolated from a Brazilian Medicinal Plant, *Myroxylon peruiferum*. The isolation bioassay-guided and the characterization of an active anti-*H. pylori* constituent was performed using the methanol extract of plant of minute amount. The active compound was identified as cabreuvin (1), an isoflavone derivative. The structure-activity relationships of several related compounds were also investigated.

McDougall C.J., Franklin L.E., Gresle S.O. & Long M.A. (2005) "Management of Radiation Dermatitis in a Patient After Mastectomy." *J Wound Ostomy Continence Nurs.* **32**(5), 337-339. [Abstract](#). Women who are diagnosed with breast cancer and undergoing chemotherapy and radiation are at high risk of developing acute radiation dermatitis. The purpose of this case study is to explore an alternative topical therapy for skin toxicity in the post-radiation care of a patient with a history of breast cancer. The patient, a 54-year-old white female, was treated by modified

radical mastectomy, chemotherapy, and radiation. During post-radiation therapy the patient developed wet desquamation reaction over the midincision line into the right axilla. Balsam Peru, hydrogenated castor oil, trypsin (Xenaderm Healthpoint, San Antonio, Tex) was trialed to evaluate efficacy in providing wound healing to the denuded skin. Within 14 days of treatment, the area was completely healed and topical therapy stopped. This case study provides the basis for further research into the area of topical therapy for women with moist desquamation after radiation for breast cancer.

Maas-Irslinger R., Hensby C.N. & Farley K.N (2003) "Experimental Methods to Demonstrate the Efficacy and Safety of Xenaderm™ Ointment: A Novel Formulation for Treatment of Injured Skin due to Pressure Ulcers" *Wounds* **15**(3), Suppl. March 2003.

Narayanan S., Van Vleet J., Strunk B., Ross R.N. & Gray M. (2005) "Comparison of Pressure Ulcer Treatments in Long-term Care Facilities: Clinical Outcomes and Impact on Cost." *J Wound Ostomy Continence Nurs.* **32**(3), 163-170. [Abstract](#). This study compared clinical outcomes and nursing labor costs associated with (a) balsam Peru, hydrogenated castor oil, and trypsin (BCT) ointment; (b) BCT + Other; and (c) Other treatments in 2014 wound episodes occurring in 861 patients (mean 2.34 wounds/patient). Treatment with BCT ointment or BCT + Other was associated with a higher healing rate ( $P < .05$ ). No Stage 1 or 2 ulcer treated with BCT ointment progressed, compared with 13.8% treated with BCT + Other and 13.4% treated with Other. The reported mean duration of treatment and time to heal were shorter for ulcers treated with BCT ointment, but differences did not reach significance, possibly because of the variability in reported treatment times. Mean daily nursing labor costs were lower for treatment with BCT than Other (\$50.8 vs \$61.7,  $P < .05$ ). These data suggest that treatment of Stage 1 or 2 ulcers with BCT may be associated with shorter treatment time and time to heal and a potential reduction in treatment-related nursing labor costs.

Noble T.A., Carr D.S., & Gonzalez M.F. (1989) "Use of a trypsin, Peru balsam, and castor oil spray on the oral mucosa: case report and review of the literature." *Pharmacotherapy.* **9**(6), 386-8. [Abstract](#). Granulex is an aerosolized spray (Dow B. Hickman Pharmaceuticals, Sugar Land, TX 77487) that contains trypsin, Peru balsam, and castor oil. It has been available for many years as a topical spray for the treatment of decubitus ulcers. We used Granulex to promote tissue healing of a necrotic ulcer of the oral mucosa in a patient with advanced oropharyngeal squamous cell carcinoma.

Prosea: *Plant Resources of South-East Asia 18: Plants producing Exudates* pp 130-131.

Walker G.T. (1968) "Balsam of Peru." *Perfumery & Essential Oil Record* **59**, 705-707.

Yucel V.E., Basmajian J.V. (1974) "Decubitus ulcers: healing effect of an enzymatic spray." *Arch Phys Med Rehabil* **55**, 517-519.

### **Botany / Economic Botany of Peru Balsam.**

Bergemann J. (1950) "The Peru balsam. 2. Parent stock; morphology, anatomy, physiology." *Pharmazie.* **5**(8), 397-402.

Bergemann J. (1950) "The Peru balsam. 3. Peru balsam; commercial names, history, extraction and preparation." *Pharmazie* **5**(9), 450-5.

Bergemann J. (1950) "The Peru balsam. 4. Products of the Peru balsam tree: Peru balsam, the balsam of the husks, the wood." *Pharmazie.* **5**(10), 494-8.

Bergemann J. (1950) "The Peru balsam. 5. Conditions of growth, and cultivation." *Pharmazie.* **5**(11), 548-53.

Coppen (1995) *Gums, Resins & Latexes of Plant Origin* FAO Series Non Wood Forest Products No 6 FAO, Geneva

Hanbury, D. (1964) "Additional note on the manufacture of balsam of Peru." *Pharmaceutical Journal* 2nd, Series V, 315-317.

Retamar J.A. (1986) "Essential oils from Argentinian Aromatic trees, Shrubs and Herbs" in Ch3. 'Essential oils from Aromatic Species' in *On Essential Oils* ed. James Verghese pub. Synthite Kolenchery, India 1986 p 170.

Poucher W.A. (1924) *American Perfumer* p427.

Poucher W.A. (1991) *Perfumes, Cosmetics & Soaps Vol 1 The Raw Materials of Perfumery* Blackie Academic & Professional 9<sup>th</sup> edn. p270-271.

Walter, E. (1916) *Manual for the Essence Industry* John Wiley.

### **Chemistry of Peru Balsam.**

Biemer T.A., Asral N. & Albanese J.A. (1992) "Simultaneous, stability-indicating capillary gas chromatographic assay for benzocaine and the two principal benzyl esters of Balsam Peru formulated in a topical ointment" *Journal of Chromatography A* **623**(2), 395-398. **Abstract.** A capillary gas chromatographic assay is presented for the determination of benzocaine and benzyl esters of Balsam Peru in a pharmaceutical preparation. The method is stability-indicating and allows for simultaneous assay of benzocaine in the presence of the non-polar Balsam esters.

Gao Y., Liu B., Zhu X., Shi L., Chen J., Gong M. & Zhang L. (1999) "Analysis of chemical components of essential oil in Peru balsam balm tree extract by GC/MS" *Analytical Instrumentation – Beijing* **3**(121), 37-38. **Abstract.** A capillary gas chromatographic assay is presented for the determination of benzocaine and benzyl esters of Balsam Peru in a pharmaceutical preparation. The method is stability-indicating and allows for simultaneous assay of benzocaine in the presence of the non-polar Balsam esters.

Glash H. & H. Wagner H. (1974) *Deutsch. Apoth. Ztg.* **114**, 45-49.

Guenther E. (1952) "Oil of balsam Peru". pp 212-220. In *The Essential Oils*, Vol. 5. New York: Van Nostrand Co.

Hausen B.M., Evers P., Stowe H., Konig W.A., & Wollenweber E. (1992) "Propolis allergy IV. Studies with further sensitizers from propolis and constituents common to propolis, poplar buds and balsam of Peru." *Contact Dermatitis* **26**, 34-44. **Abstract.** 26 different compounds have been investigated experimentally for their sensitizing capacity in guinea pigs. 19 of these occur in propolis as well as in poplar bud exudates, and 14 of them are also found in balsam of Peru. 4 caffeates and benzyl isoferulate were found to be strong sensitizers. 7 compounds were moderate, and 13 compounds showed only weak sensitizing potency. Methyl cinnamate was negative. Patch tests in 11 propolis-sensitive patients once more revealed 3-methyl-2-butenyl caffeate and phenylethyl caffeate as the major sensitizers. In addition to the 8 compounds already known to occur in propolis as well as in balsam of Peru, we detected 5 further substances that both materials have in common. Among these, benzyl isoferulate is considered a noteworthy sensitizer. Coniferyl benzoate, which was shown to be a moderate sensitizer, is present in fresh samples of balsam of Peru, while in propolis it has been detected only once so far. The flavonoid aglycones occurring in poplar bud exudates, and hence also in propolis, are weak sensitizers which play only a minor role in propolis hypersensitivity.

Hausen B.M., Simatupang T., Bruhn G., Evers P. & Koenig W.A. (1995) "Identification of new allergenic constituents and proof of evidence for coniferyl benzoate in balsam of Peru," *Am J Contact Dermat* **6** (4), 199-208. **Abstract.** Background: Balsam of Peru is used worldwide for different purposes. Three quarters of its constituents are still unknown, and its main allergens have not been identified to date. Objective: Chemical examination of balsam of Peru and experimental sensitization was performed to identify the main sensitizers. Methods: Using different analytic methods such as thin-layer chromatography, high-pressure liquid

chromatography, gas chromatography/mass spectrometry, and sensitization experiments in guinea pigs resulted in the identification of a greater number of constituents and the determination of their sensitizing potency. Results: Benzyl isoferulate, coniferyl cinnamate, hydroconiferyl cinnamate, and hydroconiferyl benzoate were identified among others as new constituents. Also, the presence of coniferyl benzoate could be shown for the first time. It showed the strongest sensitizing capacity of all compounds tested followed by benzyl isoferulate. The latter is a significant cross-linking allergen because it occurs in propolis as well. Conclusion: New sensitizing constituents have been identified in balsam of Peru. Based on these results, a patch test series has been created that is recommended for epicutaneous tests in balsam of Peru-positive patients.

Senior A. (1881) "The adulteration of balsam of Peru." *Analyst* **6**, 204-205.

### **Peru Balsam: Reviews; Comments; Theses.**

Amado A. & Taylor J.S. (2006) "Balsam of Peru or Balsam of El Salvador?" *Contact Dermatitis* **55**(2),119. **Cropwatch comments** The authors take issue with Hjorth's statement (Hjorth 1961) that the misnomer 'Peru balsam' arises from El Salvador belonging to the Viceroyalty of Peru (it didn't), but rather because Peru balsam was shipped from the port of Callao in Lima, Peru].

Api A.M. (2006) "Only Peru Balsam extracts or distillates are used in perfumery." *Contact Dermatitis* Mar 2006 **54**(3), 179. **Cropwatch comments:** According to Api - of RIFM - Peru balsam "has not been used in perfumery since 1982 when IFRA first banned this material in perfumery", and that a 0.4% concentration limit in fragrances for Peru extracts/distillates has been in place since 1991. These dates correspond to a decline in the annual volumes of Peru balsam exported from San Salvador, a reduction of the size and condition of the Peru forest, and increasing hardship for families economically dependent on work from Peru balsam production in San Salvador. However Api also reveals that unpublished murine local lymph node assay studies gives EC3 values of 4.0% for Peru balsam oil and 2.5% for Peru balsam absolute (weak to moderate sensitizer), against < 0.5% for PB (RIFM unpublished data). No proposal for relaxation of the limits for Peru balsam oil in fragrances has yet been forthcoming from IFRA in the light of these studies.

Friedländer G: "Entwicklungsgeschichtliche Untersuchungen im Gebiet der Pharmakoanatomie und Pharmakochemie". Thesis, Bern (Switzerland), 1927

Hammond C.V. (1999) "Wounds and the "Magic" Balsam" *Pharmaceutical Journal* **263** (7076), 992-993.

### **Sensitisation & Other Adverse Effects.**

Aalto-Korte K., Limaa J. Va., Henriks-Eckerman M.-J. & Jolanki R. (2005) "Allergic contact dermatitis from salicyl alcohol & salicylaldehyde in aspen bark (*Populus tremula*)." *Contact Dermatitis* **52**, 93-95, **Abstract**. Salicyl alcohol or 2-methylolphenol is a well-known allergen in phenol-formaldehyde resins and a strong sensitizer in guinea pigs. There is 1 previous report of allergic contact dermatitis from salicyl alcohol in aspen bark. We describe a second case with concomitant allergy to salicylaldehyde. An elk researcher who had handled leaves from various trees presented with eczema of the hands, face, flexures, trunk and extremities. Patch testing showed sensitivity to salicyl alcohol, salicylaldehyde, balsam of Peru (*Myroxylon pereirae* resin), aspen wood dust and an extract prepared from the bark of aspen (*Populus tremula*). Weaker reactions were observed to bark extracts of rowan (*Sorbus aucuparia*), tea-leaved willow (*Salix phylicifolia*) and goat willow (*Salix caprea*). We analysed salicyl alcohol and salicylaldehyde in the bark extracts and found the 2 chemicals in equal amounts, about 0.9 mg/mg in aspen bark and in lower concentrations in rowan and the willows. We did not find either of the chemicals in the test substance of balsam of Peru (*Myroxylon pereirae*). Besides salicyl alcohol, salicylaldehyde is also recommended to be used to screen for contact allergy to aspen. Both of these chemicals should be tested in forest workers in areas where aspen is growing.

Avalos-Peralta P., Garcia-Bravo B. & Camacho F.M. (2005) "Sensitivity to *Myroxylon pereira* resin (balsam of Peru). A study of 50 cases." *Contact Derm.* **52**(6), 304-6. [Abstract](#). The *Myroxylon pereirae* resin (MP; balsam of Peru) is a natural resin used in the local treatment of burns and wounds. *M. pereirae* extracts and distillates are very often contained in a wide range of cosmetic products and causes frequently allergic contact dermatitis - to the extent of being considered an allergy marker to perfumes. We have carried out a retrospective study of 863 patients who have been submitted to patch tests from January 2002 to June 2004. A total of 50 patients were positive to MP. Thus, the prevalence was 5.79%, slightly higher in men (7.32%) than in women (4.91%). The positive patch tests were relevant in 64%. Over the last years, it appears that there is a clear increase of the prevalence of the sensitization to MP in all the studies published. We observe an increase of the prevalence especially in aged patients, where the sensitization is linked with the use of topical medications secondary to stasis dermatitis. The high frequency of allergy to MP in our area might be associated with manipulation of citrus fruits. The increasing use of cosmetic products by the male population can also be held responsible for the higher sensitization rate in this group of patients.

Baer, R. L., Ramsey, D. L. & Biondi, E. (1973). "The most common contact allergens." *Archs Derm.* **108**, 74. [Cropwatch comments](#): cited by Opdyke (1974) : Peru balsam is among the most common contact allergens, accounting for 7.9%, reactions among 340 patients tested

Bedello P.G., Goitre M. & Cane D. (1982) "Contact dermatitis & flare from food flavouring agents." *Contact Dermatitis* **8**(2), 143-144.

Belsito D.V., Fowler J.F. Jr., Sasseville D., Marks J.G. Jr., De Leo V.A. & Storrs F.J. (2006) "Delayed-type hypersensitivity to fragrance materials in a select North American population." *Dermatitis* **17**(1), 23-8. [Abstract](#). BACKGROUND: In published reports from Europe, 3- and 4-(4-hydroxy-4-methylpentyl)cyclohexene-1-carboxaldehyde (HMPCC) (Lyrall) has been described as a common cause of allergic contact dermatitis (ACD). In Europe, the rates of reaction to HMPCC among patients undergoing patch testing for suspected ACD have varied from 1.2 to 17.0%, depending on the country. Data on the incidence of sensitivity to HMPCC among North Americans with suspected ACD have not been reported. OBJECTIVES: The goals of this study were (1) to assess the incidence of delayed-type hypersensitivity reactions to HMPCC among patients undergoing patch testing for evaluation of eczematous dermatitis at six centers throughout North America; (2) to determine the most appropriate concentration of HMPCC to use in performing patch tests; and (3) to compare and contrast the incidence rates for HMPCC hypersensitivity to those for other fragrance materials screened with the North American Contact Dermatitis Group (NACDG) screening tray, which includes fragrance mix, *Myroxilon* (sic) *perreira* (balsam of Peru), cinnamic aldehyde, ylang ylang oil, jasmine absolute, and tea tree oil. METHODS: This report represents the prospective multicenter data on patients tested with the fragrance-related allergens on the NACDG standard screening tray and with HMPCC at 5%, 1.5%, and 0.5% concentrations in petrolatum. Statistical analyses were performed with Student's t-test (two tailed) and the chi-square test. RESULTS: Data from 1,603 patients evaluated at five US sites and one Canadian site were analyzed. Most patients (87.8%) were Caucasian. The majority (67%) were women, and 26.2% had a history consistent with atopic dermatitis. The patients ranged in age from 1 to 88 years, and the mean +/- standard deviation was 46.3 +/- 16.5 years. Myroxylon pereirae (balsam of Peru) and fragrance mix were the most frequent patch-test-positive fragrance allergens (6.6% and 5.9%, respectively). Cinnamic aldehyde (1.7%), ylang ylang oil (0.6%), jasmine absolute (0.4%), HMPCC (0.4% for 5% HMPCC, 0.3% for 1.5% HMPCC, and 0.2% for 0.5% HMPCC), and tea tree oil (0.3%) less frequently yielded positive reactions. Men were more likely than women to be allergic to cinnamic aldehyde. Women were more likely than men to be allergic to jasmine absolute. Atopic patients were no more likely to react to fragrance materials than were nonatopic patients. Patients who reacted to jasmine absolute tended to be older than the general population whereas those who reacted to tea tree oil tended to be younger than the general population. There were no other demographic differences between patients who reacted to a given fragrance material and the entire population studied. Testing with fragrance mix and balsam of Peru failed to identify the majority of patients in this

study who were found to be sensitized to jasmine absolute, HMPCC, or tea tree oil. CONCLUSION: HMPCC is an uncommon allergen in the North American population. We recommend testing with 5% HMPCC in petrolatum for those patients suspected of having a fragrance allergy.

Bjarnson B., Flosadottir E. & Fischer T. (2000) "Assessment of Peru patch tests" *Contact Dermatitis*. **42**, 326-329. [Abstract](#). To find an ideal test technique for as low a dose of balsam of Peru (*Myroxylon pereirae*) as possible, subjects testing positive to balsam of Peru are re-tested with a 25% concentration of balsam of Peru in petrolatum. Applications are with Finn Chambers for 6 different application times, and directly by foils for 96 h (4 days (D)). The goals are to confirm which subjects are positive and which are not, and, using that information, to see if it is possible to distinguish between these 2 groups, tested concomitantly at much lower serial dose levels, in terms of perfusion or by visual assessments. 5 different serial doses are applied with strips for 3-96 h (4D) and with foils for 96 h (4D). The Finn Chamber tests allow a distinction between visually positive and negative subjects supported by perfusion assessments. With the foils, a 24x lower serial dose level than with the 25% test substance is sufficient to distinguish between positive and negative subjects in terms of perfusion values. This approach requires readings up to 9 days. With this test, the visual approach yields only 3 of 10 positive subjects. This study demonstrates that a lower test dose is possible with perfusion assessments compared to visual ones.

Bjarnason B, Flosadottir E. & Fischer T. (2000) "Effect of dark test-substance pigmentation on skin perfusion assessments and effect of test technique on balsam of Peru patch-test results." *Contact Dermatitis*. **42**(6), 318-25. [Abstract](#). 13 balsam of Peru (*Myroxylon pereirae*) patch-test-positive subjects are re-tested with 25% balsam of Peru in petrolatum and with serial doses printed on polyester squares. All substances are applied with tape strips for 3, 6, 24 (1 day [D]), 48 (2D), 72 (3D) and 96 h (4D) on each subject and for 96 h (4D) with plastic foils. Tests are followed visually and with perfusion assessments from 3 h to 9 days. Results show that pigment remnants following detachment of patches affect perfusion assessments. Such effect due to pigment is supported by readings of patch tests through the petrolatum test substance while applied with transparent foils. For most reactions, good agreement is observed between the assessment techniques when peak assessment values of reactions are compared. There is inter-individual variation in perfusion with identical tests. With the petrolatum test substance, increased visible reactivity was observed when the application time was extended up to 24 h (1D), while extension of application time increased perfusion in most cases except for an extension from 24 (2D) to 48 h (4D) where decreased perfusion resulted in most cases. Dose and application time did not affect the timing of highest reactivity of reactions in most cases.

Bonnevie P. (1939) "Atiologie und Pathogenese der Ekzemkrankheiten. Leipzig":*J.A Barth* 174-180, 1939

Blondeel A., Oleffe J. & Achten G. (1978) "Contact allergy in 330 dermatological patients." *Contact Dermatitis* **4**, 270-276.

Breit R. (1972) "Medikamentöse Kontaktallergie beim Ekzero und Geschwür des Unterschenkels." *Munch Med Wschr* **114**, 22-27.

Brun R. (1982) ["Evolution of contact dermatitis factors in a population.Epidemiology 1975-1981"] *Dermatologica*. **165**(1), 24-9 [Abstract](#). Comparative results between positive patch tests found during the periods 1968-1974 and 1975-1981 are presented. The number of sensitised patients to nickel, chromate and Peru balsam has significantly increased. On the other hand, the number of turpentine-oil-positive patch tests has strongly decreased. This mirrors the drop in the imported quantities of this product. A schema concerning factors influencing the apparent allergenicity is given.

Bruze M. (1986). "Simultaneous reactions to phenol-formaldehyde resins colophony/hydroabietyl alcohol and balsam of Peru/perfume mixture." *Contact Dermatitis*. **14**(2), 119-20.

Bruynzeel D.P., van den Hoogenband H.M. & Koedijk F. (1984) "Purpuric vasculitis-like eruption in a patient sensitive to balsam of Peru." *Contact Dermatitis* **11**(4), 207-9. [Abstract](#). A case is reported of secondary dissemination of allergic contact dermatitis in a patient sensitive to balsam of Peru. The primary eruption was located in the face. The secondary lesions appeared as purpuric vasculitis-like eruptions on both legs. Such an unusual manifestation of contact dermatitis may cause considerable delay in establishing the correct diagnosis.

Calnan C.D. (1975) "Active sensitization to para and balsam of Peru." *Contact Dermatitis* **1**(2), 126-7.

Calnan C.D. (1975) "Resorcinol monobenzoate" *Contact Dermatitis* **1**, 59-60.

Cancian M, Fortina A.B. & Peserico A. (1999) "Contact urticaria syndrome from constituents of balsam of Peru and fragrance mix in a patient with chronic urticaria." *Contact Dermatitis* **41**(5), 300.

Case, Edgar 'Balsam of Peru'. The Cayce Herbal: A Comprehensive Guide to the Botanical Medicine of Edgar Cayce (available from <http://www.meridianinstitute.com/echerb/Files/1balsamp.html>).

Calap Calatayud J. (1968) "Does there exist a specific occupational occurrence of allergic dermatitis due to balsam of Peru (B. P.)?" *Actas Dermosifiliogr.* **59**(5), 365-7.

De Carvalho, L.P. (1956) Dos alergenos de contato nas profissoes. *Brasil. Med.* **70**, 77. **Cropwatch comments:** Contact dermatitis reported from the tree wood of *Myroxylon pereirae*.

Le Coz C.J. (2001) "Hypersensitivity to balsam of Peru (*Myroxylon pereirae*)" *Ann Dermatol Venereol* **128**(1), 71-2.

Cummer C.L. (1927) "Dermatitis produced by balsam of Peru." *Arch Dermatol* **16**, 44-50.

Dickel H., Kuss O., Schmidt A. & Diepgen T. (2002) "Occupational relevance of positive standard patch-test results in employed persons with an initial report of an occupational skin disease." *International Archives of Occupational and Environmental Health* **75**(6), 423-434. [Abstract](#). Objectives. It is commonly accepted that the standard screening tray is an essential diagnostic test in patch testing supporting the diagnosis of contact dermatitis, the most common type of occupational skin disease (OSD). In this study standard patch-test results of employed persons with an initial report of an OSD were analyzed within 24 occupational groups. Methods. An evaluation was made of employed persons recorded in the Register of Occupational Skin Diseases in Northern Bavaria (Berufskrankheitenregister Haut-Nordbayern; BKH-N) between 1990 and 1999, catering for those standard screening tray allergens tested over the 10-year period. Results. Nickel sulfate was the most common sensitizer (29.5%), showing occupational relevance in only 11% of the cases sensitized. Other common sensitizers were cobalt chloride (13.5%), p-phenylenediamine free base (10.7%), potassium dichromate (9.8%), fragrance mix (5.4%), thiuram mix (4.2%), balsam of Peru (4.0%), chloromethylisothiazolinone/methylisothiazolinone (4.0%), and formaldehyde (4.0%). The most occupationally relevant sensitizers were thiuram mix (71%), epoxy resin (67%), p-phenylenediamine free base (59%), p-phenylenediamine-black-rubber mix/N-isopropyl-N'-phenyl-p-phenylenediamine (53%), potassium dichromate (48%), formaldehyde (38%), chloromethylisothiazolinone/methylisothiazolinone (37%), and mercapto-mix/mercaptobenzothiazole (35%). Occupational groups at risk of acquiring delayed-type sensitization were, in particular, electroplaters, tile setters and terrazzo workers, construction and cement workers, solderers, wood processors, and leather and fur processors. Conclusions. The standard series contributes valuable information and asserts its position in clarifying the causes of OSDs. Based on the study results, the rate of occupationally relevant sensitization to each single allergen is demonstrated, and the difficulties in verifying the occupational relevance are discussed.

Dogra A., Minocha Y.C., Sood V.K. & Dewan S.P. (1994) "Contact dermatitis due to cosmetics and their ingredients." *Indian Journal of Dermatology, Venerology & Leprosy* **60**(2), 72-75. [Abstract](#). Patches of common cosmetics like lipstick, sindhoor, cold cream, eyebrow pencil, rouge, bindi and their ingredients including methyl paraben, colophony, para phenylene diamine, balsam peru, cetostearyl alcohol, formaldehyde, lanolin, beeswax and liquid paraffin were applied in 200 females. Ingredients of cosmetics showed more frequent sensitivity as compared to the cosmetics applied as such. Para-phenylene diamine (35%) being the most common allergen followed by balsam peru (22.5%) and parabens (19.25%). The least common allergen was liquid paraffin (0.5%). Among cosmetics, the most common agent was sindhoor (5.5%) followed by lipstick (5.1%) cold cream (3.75%) rouge (2%), bindi (1.75%) and eyebrow pencil (1.5%).

Ebner H. (1974) "Peruvian balsam and perfumes. Studies on allergologic relations between these substances" *Hautarzt* **25**, 123-126.

Ebner H. & Lindemayr H. (1977) "Ulcus cruris und allergisches Kontaktekzem." *Wien Klin Wschr* **89**,184-188, 1977.

Eberhartinger C. (1984) "Beobachtungen zur Häufigkeit von Kontaktallergien." *Z Hautkr* **59**,1283-1289, 1984.

Edman B (1994) "The influence of shaving method on perfume allergy" *Contact Dermatitis* **31**(5), 291. [Abstract](#). Among men, the most frequent contact allergens are perfumes (fragrance mix and balsam of Peru). Considering that the main cause of nickel allergy is ear-piercing, shaving with a razor blade might be the cause of perfume contact allergy, by creating small wounds that increase the penetration of applied perfume substances derived from soaps, shaving foams and after-shave lotions. 19 males with contact allergy to fragrance mix and/or to balsam of Peru were interviewed about their shaving habits by letter. 17 responded (89%), of whom 12 (71%) had been using razor blades continuously for a period of at least 1 year. At our clinic, the frequency of razor blade usage was found to be 45% in patch tested men without perfume contact allergy. When comparing the frequencies of razor blade usage among patch tested men with and without perfume contact allergy, there was a statistically significant over-representation ( $p = 0.047$ ) among those with perfume allergy. The risk of perfume allergy when using razor blades was found to be 2.9 (odds ratio).

Fisher A.A. (1974) "The clinical significance of positive patch test reactions to balsam of Peru." *Cutis* 1974.

Fisher A. A. (1973). "Allergic reaction to femininc hygiene sprays." *4robs Derm.* **108**, 801.

Fisher A.A. (1990) "Perfume dermatitis in children sensitized to balsam of Peru in topical agents." *Cutis* **45**(1), 21-3. [Abstract](#). Hjorth in his classic monogram "Eczematous Allergy to Balsams" emphasized that sensitization to balsam of Peru is most important since secondary allergens such as "fragrances" are ubiquitous. The application of a topical medication containing balsam of Peru to the skin of an infant, particularly in the occluded diaper area, seems a great way to sensitize the infant not only to balsam of Peru but also to our fragrant environment.

Forsbeck M. & Skog E. (1977) "Immediate reactions to patch tests with balsam of Peru." *Contact Dermatitis* **3**(4), 201-5. [Abstract](#). Closed patch tests with balsam of Peru gave rise to nine immediate reactions among 121 patients with different dermatoses and to 10 reactions among 57 patients with chronic urticaria. Among compounds of balsam of Peru, cinnamic aldehyde, cinnamic acid benzoic acid and benzaldehyde also gave the same reactions. The reactions could not passively be transferred with serum from patients. They were abolished by antihistamine given before testing, and by pretreatment with compound 48/80. Balsam of Peru and cinnamic aldehyde did not provoke new symptoms when given orally to patients.

Foussereau J., Malville J., Grosshans J., *et al* (1968) "Effects allergisants du pin." *Bull Soc Franc Dermatol* **75**, 697-699.

Fregert S. & Rorsman H. (1962) "Simultaneous hypersensitivity to balsam of pine and to balsam of Peru." *Acta Derm Venereol.* **42**, 21-2.

Fregert S. & Moller H. (1963) "Contact allergy to balsam of Peru in children." *Br J Dermatol.* **75**, 218-20.

Friis, B. & Hjorth, N. (1973) "Immediate reactions to patch tests with balsam of Peru" *Contact Dermatitis Newsletter* (13), 389.

Gehring W. & Gloor M. (1988) "Iatrogene Sensibilisierung". *Dt Dermatol* **36**, 116-124.

Gautron G. (1969) "Allergy to Peruvian balsam." *Bull Soc Fr Dermatol Syphiligr* **76**(1), 34-7.

Glasl H, & Wagner H (1974) "Gaschromatographische Untersuchung von Arzneibuchdrogen. I. Perubalsam." *Dt Apoth Ztg* **114**, 45-49.

De Groot A.C. & Frosch P.J. (1998) "Fragrances as a Cause of Contact Dermatitis in Cosmetics: Clinical Aspects & Epidemiological Data." In *Fragrances: Beneficial & Adverse Effects* eds P.J. Frosch, J.D. Johansen & I.R. White Springer-Verlag (1998).

Gudmundsen K.J., Murphy G.M., O'Sullivan D., *et al* (1991) Polymorphic light eruption with contact and photocontact allergy." *Br.J. Dermatol* **124**, 379-382.

Hammershoy O. (1980) "Standard patch test results in 3225 consecutive Danish patients from 1973 to 1977". *Contact Dermatitis* **6**, 263-268.

Hasan T., Rantanen T., Alanko K., Harvima R.J., Jolanki R., Kalimo K., Lahti A., Lammintausta K., Lauerma A.I., Laukkanen A., Luukkaala T., Riekkii R., Turjanmaa K., Varjonen E., Vuorela A.M. (2005) "Patch test reactions to cosmetic allergens in 1995-1997 and 2000-2002 in Finland--a multicentre study." *Contact Dermatitis* **53**(1), 40-5. [Abstract](#). Contact sensitivity to cosmetics is common, but the sensitizing chemicals vary between countries and study periods. The present survey aimed at revealing the recent trends in patch test sensitivity with cosmetic chemicals in Finland. We report a retrospective multicentre survey of patch test reactions focusing on cosmetic-related substances and comparing the test results in 1995-97 with those in 2000-02. The most striking increases in the frequency of the patch test sensitivity were found with balsam of Peru and propolis from 4.0% to 6.2% ( $P < 0.001$ ) and from 0.5% to 1.4% ( $P < 0.001$ ), respectively, whereas the most prominent decreases were found with methylchloro/methylisothiazolinone and chlorhexidine diglucuronate from 2.4% to 1.3% ( $P < 0.001$ ) and from 1.2% to 0.5% ( $P < 0.001$ ), respectively. The level of patch test sensitivity to methyldibromo glutaronitrile increased, although not significantly, from 1.0% to 1.5%. An increasing tendency was also found with hair dye chemicals 4-aminophenol and toluene-2,5-diamine or toluene-2,5-diamine sulfate from 1.3% to 3.8% and from 1.4% to 5.2%, respectively, while such a tendency was not found among permanent wave chemicals. The sensitivity level of fragrance mix remained the same (6% - 7%). We conclude that surveys revealing the state of sensitivity to cosmetic chemicals should be performed periodically in different countries.

Hausen B.M., Simatupang T. & Kunze B. (1990) "Perubalsamallergie bei einem Bauschlossler." *Akt Dermatol* **16**, 196-201.

Hausen B.M. & Angel M. (1992) "Studies on the sensitizing capacity of imidazole and triazole derivatives. Part II." *Am J Contact Dermatitis* **3**, 95-101.

Hausen B.M. (2001) "[Smoking, a Sweet Tooth, and Balsam of Peru - A circulus vitiosus?]" *Aktuel. Dermatol* **27**(5), 136-143 [Abstract](#). Smoking, a Sweet Tooth, and Balsam of Peru - A Circulus Vitiosus In several countries allergic reactions to balsam of Peru (BP) have now made it the third most common contact allergen. With its approximately 250 constituents BP functions as an important indicator in the standard series for substances which occur simultaneously in

cigarettes, pharmaceutical products and certain sweet foods. The doctor's final discussion with the patient on a positive test result to BP remains obscure when the patient is concealed only about BP itself and its possible implication in fragrance allergy. The additional testing of BP constituents, however, bears the advantage of giving the patient more specific details on the etiology of his allergy and the importance of certain similar allergens e.g. in cream toffees, fruit gums, icecream, chewing gum and sweet beverages like Coca-Cola® and vermouth. In the case report presented here a 56-year-old employee of a shipping company used to smoke up to 60 cigarettes per day and drink up to three liters of Coca-Cola® daily. She suffered from allergic contact dermatitis located at the edge of the forefinger and thumb of both hands since one and a half years. She was allergic to balsam of Peru (+-plus in the standard series) and gave a +++-plus reaction to coniferyl benzoate in the epicutaneous test with a BP series consisting of 25 typical allergenic BP-constituents. Complete healing was obtained through avoiding Coca-Cola® and leasung to smoke. Relapses occurred after consumption of cream toffees and fruity boiled sweets. Supposingly balsam of Peru and the caramellic part of certain sweets share the same (coniferyl benzoate?) or chemically related compounds which must be made responsible for the skin lesions observed after their ingestion.

Hausen B.M. (2001) "Contact allergy to balsam of Peru. II. Patch test results in 102 patients with selected balsam of Peru constituents". *Am. J. Contact Derm.* **12**(2), 93-102. [Abstract](#). Smoking, a Sweet Tooth, and Balsam of Peru - A Circulus Vitiosus In several countries allergic reactions to balsam of Peru (BP) have now made it the third most common contact allergen. With its approximately 250 constituents BP functions as an important indicator in the standard series for substances which occur simultaneously in cigarettes, pharmaceutical products and certain sweet foods. The doctor's final discussion with the patient on a positive test result to BP remains obscure when the patient is concealed only about BP itself and its possible implication in fragrance allergy. The additional testing of BP constituents, however, bears the advantage of giving the patient more specific details on the etiology of his allergy and the importance of certain similar allergens e.g. in cream toffees, fruit gums, icecream, chewing gum and sweet beverages like Coca-Cola® and vermouth. In the case report presented here a 56-year-old employee of a shipping company used to smoke up to 60 cigarettes per day and drink up to three liters of Coca-Cola® daily. She suffered from allergic contact dermatitis located at the edge of the forefinger and thumb of both hands since one and a half years. She was allergic to balsam of Peru (+-plus in the standard series) and gave a +++-plus reaction to coniferyl benzoate in the epicutaneous test with a BP series consisting of 25 typical allergenic BP-constituents. Complete healing was obtained through avoiding Coca-Cola® and leasung to smoke. Relapses occurred after consumption of cream toffees and fruity boiled sweets. Supposingly balsam of Peru and the caramellic part of certain sweets share the same (coniferyl benzoate?) or chemically related compounds which must be made responsible for the skin lesions observed after their ingestion.

Hjorth N. (1959) "Eczematous allergy to Balsam of Peru and allied natural resins." *Presentation to the European Congress of Allergy*. London. Sept 3<sup>rd</sup> 1959.

Hjorth N. (1961) "Eczematous allergy to balsams." in *Allied Perfumes and Flavouring Agents*. Copenhagen: Munksgaard, 1961: pp94-96.

Hjorth N. (1961) "Eczematous allergy to balsams, allied perfumes and flavouring agents, with special reference to balsam of Peru." *Acta Derm Venereol* **41** (suppl 46), 1-216.

Hjorth N. (1982) "The Prosser-White Oration 1980: Skin reactions to balsams and perfumes." *Clinical and Experimental Dermatology* **7**(1), 1.

Horsch W. & Wedler D. (1959) "Preparation of an emulsion containing Peru balsam with special consideration to Tween 20." *Pharmazie* **14**(2) Suppl 2, 21-4.

Jacob S.E. & Stechschulte S.(2008) "Eyelid dermatitis associated with balsam of Peru constituents: benzoic acid & benzyl alcohol." *Contact Dermatitis* **58**(2), 111-2.

Johansen J.D., Andersen T.F., Veien N., Avnstorp C., Andersen K.E. & Menne T. (1997) "Patch testing with markers of fragrance contact allergy. Do clinical tests correspond to patients' self-reported problems?" *Acta Derm Venereol* **77**(2), 149-53. [Abstract](#). The aim of the present study was to investigate the relationship between patients' own recognition of skin problems using consumer products and the results of patch testing with markers of fragrance sensitization. Eight hundred and eighty-four consecutive eczema patients, 18-69 years of age, filled in a questionnaire prior to patch testing with the European standard series. The questionnaire contained questions about skin symptoms from the use of scented and unscented products as well as skin reactions from contact with spices, flowers and citrus fruits that could indicate fragrance sensitivity. A highly significant association was found between reporting a history of visible skin symptoms from using scented products and a positive patch test to the fragrance mix, whereas no such relationship could be established to the Peru balsam in univariate or multivariate analysis. Our results suggest that the role of Peru balsam in detecting relevant fragrance contact allergy is limited, while most fragrance mix-positive patients are aware that the use of scented products may cause skin problems. **Cropwatch comments: Note conclusion: use of Peru balsam (in patch tests) of limited use in detecting relevant fragrance contact allergy.**

Jordan W.P. (1973) "Resorcinol monobenzoate, steering wheels and Peruvian balsam." *Arch Dermatol* **108**, 278.

Kalensky J. (1991) "Perubalsam allergie bei Ulcus cruris-Patienten." *Csl Dermatol* **66**, 5-9.

Katona M. & Egyud K. (2001) "Increased sensitivity to balsams and fragrances among our patients" *Orv. Hetl.* **142**(9), 465-6. [Abstract](#). Allergic contact dermatitis caused by fragrances and balsams play an increasingly important role in the daily practice of dermatology. Based on county tests, the authors have found high increase in 1999, which is in accordance with observations made abroad and the prognosis of earlier tests. The balsam of Peru and the fragrance mix are among the leader allergens, and this should be considered during treatment. Irrespective of age, scentless and hypoallergen cosmetics are to be used.

van Ketel W.G. (1973) "Patch tests: Methodology, standardization and significance of positive results." *Arch Belg Dermatol* **29**, 73-82.

Krob H.A., Fleischer A.B. Jr., D'Agostino R. Jr., Haverstock C.L. & Feldman S. (2004) "Prevalence and relevance of contact dermatitis allergens: a meta-analysis of 15 years of published T.R.U.E. data". *J. Am. Acad. Dermatol.* **51**(3), 349-53.

Kuljanac I, Knezevic E, Cvitanovic H. (2006) "Epicutaneous patch test results in patients with allergic contact dermatitis in Karlovac county--a retrospective survey." *Acta Dermatovenerol Croat.* **14**(3),156-9. [Abstract](#). During the 1994-2003 study period, patch testing was carried out in 1102 subjects (740 female and 362 male, mean age 39.8, range 7-81 years) suspected to have allergic contact dermatitis (ACD). Epicutaneous patch test with a standard series of contact allergens was made by the Institute of Immunology, Zagreb, Croatia, according to the International Contact Dermatitis Research Group (ICDRG) rules. During the study period, 399 (36.2%) subjects with one or more positive tests were recorded, and 640 positive tests were observed. The most frequent allergens were nickel sulfate identified in 214 (33.4%), cobalt chloride in 64 (10%), fragrance mix in 60 (9.4%), wood tar in 47 (7.3%), potassium dichromate in 39 (6.1%), balsam of Peru in 29 (4.6%) and other allergens in 187 (29.2%) cases. According to the localization of ACD, hands as the most common site were involved in 535 (48.5%) cases, followed by the face in 167 (15.2%) and other locations in 400 (36.3%) cases. It is concluded that nickel is the principal allergen as the cause of ACD, mostly affecting women. The areas most frequently involved by ACD were the hands and face.

Larsen W., Nakayama H., Lindberg M., Fischer T., Elsner P., Burrows D., Jordan W., Shaw S., Wilkinson J., Marks J. Jr., Sugawara M. & Nethercott J. (1996) "Fragrance contact dermatitis: a worldwide multicenter investigation (Part I)." *1: Am J Contact Dermat.* **7**(2), 77-83. [Abstract](#).

**OBJECTIVE:** The aim of this study was to determine the prevalence of responses to selected fragrance materials in patients with suspect fragrance allergy and to evaluate risk factors and associations with such responses. The validity of using specific fragrance ingredients versus a mixture of fragrances was evaluated in terms of predicting allergy to different fragrance ingredients. **METHODS:** One hundred sixty-seven subjects were evaluated in seven centers worldwide with a fragrance mix, the eight ingredients in the fragrance mixture, six other well-known fragrance allergens, balsam of Peru, and 15 lesser studied fragrance materials. **RESULTS:** The age of the patients was 44.9 +/- 17.5 years (mean +/- SD). More than 85% were women. A relatively high proportion gave a past history of atopic disease. Facial eruptions (40%) and hand involvement (26.7%) were the most common topographic sites. All but 4 of the 35 fragrance materials produced a positive response in > 1%. A reaction to fragrance mix occurred in 47.3%. Seven of the 34 ingredients tested produced an allergic response in more than 10% of those tested. Men were more likely than women to exhibit a positive response to five fragrance ingredients. White persons were more likely to react to perfume mix (52.8% versus 25.3%) and certain ingredients in the mix than Asian persons. Allergy to benzyl salicylate was more common in Japan than in Europe or the United States. **CONCLUSION:** The age at which patients with perfume allergy present for evaluation is similar to that of other contactants. Atopic individuals may be overrepresented in this group of patients. Face involvement is likely. White persons are more likely to react to fragrance mix, whereas in Asian patients benzyl salicylate was a more frequent allergen. Fragrance mix corrected with 85.6% of positive responses to fragrance ingredients. The addition of ylang ylang oil, narcissus oil, and sandalwood oil to fragrance mix would be expected to pick up 94.2% with positive responses to fragrance materials; adding balsam of Peru increases this to 96%.

Larsen W., Nakayama H., Fischer T., Elsner P., Frosch P., Burrows D., Jordan W., Shaw S., Wilkinson J., Marks J. Jr, Sugawara M., Nethercott M., & Nethercott J. (1998) "A study of new fragrance mixtures." *Am J Contact Dermat.* 9(4), 202-6. [Abstract](#). **OBJECTIVE:** To determine the frequency of responses to four mixtures of fragrance materials in routine clinic patients undergoing patch testing for suspect allergic contact dermatitis. The validity of using fragrance mixtures alone, or in combination, was evaluated in terms of predicting allergy to fragrance judged on the basis of finding a response to at least one of the fragrance mixtures. **METHODS:** A total of 752 subjects were patch tested in five centers worldwide with (1) fragrance mix 8% (FM), (2) balsam of Peru 25%, (3) a mixture of seven of the eight FM 8% ingredients and other fragrance ingredients including jasmine absolute (jasmine/FM mix), and (4) a mixture of five selected natural fragrance ingredients (NM). **RESULTS:** Of 752 subjects, 100 (13%) had positive patch tests to at least one of the four fragrance mixtures. The age of the patients was 45.2 +/- 18.3 years (mean +/- SD). Ninety-six percent were Caucasian. Facial eruptions and hand involvement were the most common topographic sites. Of subjects exhibiting a positive response, 67% reacted to FM, 63% to the jasmine/FM mix, 47% to the NM, and 38% to balsam of Peru. Testing with FM and NM identified 84% of the perfume-allergic patients. FM 8% tested simultaneously with the jasmine/FM mix identified 86% of the perfume-allergic patients. Testing simultaneously with three test materials combining either the NM or the jasmine/FM mix with balsam of Peru and FM identified 95% of the perfume-sensitive patients. **CONCLUSIONS:** The simultaneous testing of NM or jasmine/FM mix, in addition to the conventional use of FM 8% and balsam of Peru, increases the sensitivity of testing for fragrance allergy from 81% to 95%.

Lazarov A. (2006) "European Standard Series patch test results from a contact dermatitis clinic in Israel during the 7-year period from 1998 to 2004." *Contact Dermatitis* 55(2),73-6. [Abstract](#). The results of a 7-year retrospective study (1998-2004) from patch testing with the European Standard Series (ESS) establishing the frequency of sensitization in a contact dermatitis clinic in Israel are presented. 23 allergens were patch tested on 2156 patients, 1462 females (67.8%) and 694 males (32.2%). Atopy and asthma were present in 21.9% of the patients. One or more allergic reactions were observed in 937 patients (43.5%). The highest yield of patch test positives from the 1076 positive reactions were obtained from nickel sulfate (13.9%), fragrance mix (7.1%), potassium dichromate (3.8%), Balsam of Peru (3.6%), CL+Me-isothiazolinone (3.4%) and cobalt chloride (3.4%). Allergens which produced the least amount of positive results were primin and

clioquinol. Allergic contact dermatitis (ACD) was established in 32.8%, whereas occupationally related allergic (8.0) and irritant contact dermatitis (5.6%) affected a total of 13.6% of the cases studied. The most common clinical forms of dermatitis were chronic dermatitis (47.7%) followed by acute dermatitis (22.8%), and lichenification and hyperkeratosis (7.9%). The hands (30.7%), face and neck (23.9%) and extremities (11.3%) were the most frequently affected areas. Four allergens in our study differed from the top 10 allergens in Europe namely: Cl+Me-isothiazolinone, formaldehyde, 4-tert-butylphenol formaldehyde resin and sesquiterpene lactone mix reflecting an existing difference in environmental exposure. Our study is the first to provide data on the frequency of sensitization and important allergens in the aetiology of ACD in Israel. In spite of the existing differences with Europe, we conclude that ESS is an appropriate screening system for the diagnosis of ACD in Israel.

Lehnen M., Kohaus S., Korber A., Hillen U., Grabbe S. & Dissemond J. (2006) [Contact allergies in patients with chronic wounds : Results of a study from 1999 to 2004.] *Hautarzt*. **57**(4), 303-8 [Abstract](#). Patients with chronic wounds frequently acquire clinically relevant contact sensitization. We examined the results of the skin patch tests in patients with chronic wounds, who were treated between 1999-2004 in the Department of Dermatology, University School of Medicine, Essen, Germany. Altogether 105 patients with chronic wounds underwent patch testing. In 68 individuals, contact sensitization to at least one substance was detected. The most frequent contact allergens were to balsam of Peru, Amerchol L-101, fragrance mix, wool wax alcohols and rosins. Contact sensitization to wound dressing materials was also identified in 4 patients. Our results demonstrate the current spectrum of contact sensitization of patients with chronic wounds. Our results show the importance of paying attention to the ingredients in wound dressings and performing patch testing if there is any clinical suggestion of allergic contact dermatitis.

Lintum J.C.A.Te-. & Nater J.P. (973) "On the persistence of positive patch test reactions to balsam of Peru, turpentine and nickel." *Br. J. Dermatol.* **89**(6), 629-34. [Abstract](#). SUMMARY A group of 105 patients with positive patch test reactions to turpentine, balsam of Peru or nickel were re-examined after periods of 2–15 years. Of twenty-eight patients who had shown positive patch test reactions to turpentine eighteen gave negative reactions; of twenty persons formerly positive to balsam of Peru ten had become negative. Of fifty-seven patients who had formerly been positive to nickel eighteen gave negative reactions. The implications of these findings in relation to the time factor and the possibility of avoidance of the allergen are discussed.

Ljunggren B. (1981) "Contact dermatitis to estradiol benzoate." *Contact Dermatitis* **7**, 141-144. [Abstract](#). Three patients developed facial dermatitis after contact with preparations containing estradiol benzoate. Patch tests were positive to estradiol benzoate 0.1% in MEK but negative to other related estrogens including estradiol. All three patients also had positive tests to resorcinol monobenzoate and two out of three to balsam of Peru. Most likely estradiol benzoate was the primary sensitizer.

Lynde C.W. & Mitchell J.C. (1982) "Patch testing with balsam of Peru and fragrance mix." *Contact Dermatitis* **8**(4), 274 -7.

Machet L., Couhe C., Perrinaud A., Hoarau C., Lorette G., & Vaillant L. (2004) "A high prevalence of sensitization still persists in leg ulcer patients: a retrospective series of 106 patients tested between 2001 and 2002 and a meta-analysis of 1975-2003 data." *Br J Dermatol.* **150**(5), 929-35. [Abstract](#). BACKGROUND: Sensitization to topical treatments used in leg ulcers is common. Questioning and patch testing are used to identify causative drugs or dressings. OBJECTIVES: To study the current frequency of sensitization in our centre, to analyse previously published studies, and to compare sensitization in recent years with studies published before 1990. METHODS: A retrospective study was undertaken of all patients admitted with leg ulcers in 2001 and 2002. Of the files of 235 patients with leg ulcers reviewed, we identified 106 patients (group A) who had been patch tested in our institution between 2001 and 2002 with the European standard series and an additional series. The frequency of sensitization was compared with an earlier unpublished retrospective study in our centre of 36 leg ulcer patients tested in 1988 (group B), with a group of unselected contact dermatitis patients tested between 1 January 1997 and 31

December 2000 in our centre (group C), and with results published in the literature. We performed a computerized database search of MEDLINE and compared results obtained in recent years with those obtained before 1990 to obtain evidence of changing trends. RESULTS: Seventy-five per cent of the 106 patients had at least one positive reaction, and 57% had two or more positive reactions. Balsam of Peru was positive in 40% of cases, followed by lanolin (21%), fragrance mix (18%), trichlocarban (13%), colophony (11%), Cetavlon (cetrimide cream) (9%) and neomycin (9%). Thirty-five of the 36 group B patients had at least one positive reaction. Lanolin was the most frequent (31%), followed by balsam of Peru (22%), Cetavlon (19%), colophony (14%), terebenthene (14%), quinoline mix (11%) and benzocaine (8%). Two hundred and eighty-six of 526 patients of group C were positive in at least one test (54.4%). Three allergens gave a sensitization rate >10%: balsam of Peru (12.5%), fragrance mix (15.2%) and nickel sulphate (21.1%). Review of the literature and calculation of sensitization rates in a pool of 3043 patients extracted from 24 series, plus our own, showed persistence of high sensitization rates and a significant (8.5%) increase in sensitization between the two periods compared. There was a decrease in sensitivity to lanolin, constant sensitization to aminoglycosides, a slight increase in sensitivity to thiuram mix and glucocorticoids, and a marked increase in sensitivity to balsam of Peru in France. Newer topical treatments and dressings showed very low rates of sensitivity with the exception of hydrogels. CONCLUSIONS: Despite warnings, sensitization to topical treatments for leg ulcers is still frequent and, moreover, continues to increase, some variations reflecting local nursing practices and variations in topical treatment available. Although a decrease in sensitization rate with lanolin has been observed throughout the world, no decrease in sensitization rate has been demonstrated with aminoglycosides, and sensitization to glucocorticoids, thiuram mix and new products (hydrogels) is now increasingly being reported.

Magen E., Mishal J. & Schlesinger M. (2006) "Sensitizations to allergens of TRUE test(R) in 864 consecutive eczema patients in Israel" *Contact Dermatitis* **55**(6), 370-1. [Abstract](#). The TRUE test((R)) is a widespread diagnostic tool for initial patch testing of patients with contact dermatitis (CD). From 2002 to 2005, 864 patients with eczema were patch-tested using TRUE test((R)) in one Israeli allergology clinic. 547 (63.3%) patients were female and 317 (36.7%) were male. 346 (40%) patients had  $\geq 1$  positive patch test reactions. The most common allergens were nickel sulfate for 114 (13.2%) patients, potassium dichromate 111 (12.8%), fragrance mix 59 (6.8%), cobalt chloride 12 (1.4%), ethylenediamine dihydrochloride 11 (1.3%), epoxy resin 11 (1.3%), balsam of Peru 9 (1.0%), carba mix 7 (0.8%), thiomersal 6 (0.7%), wool alcohol 5 (0.6%), black rubber (PPD) mix 5 (0.6%), neomycin 4 (0.5%); Kathon CG, Colophony and Quaternium 15 - each 2 (0.2%), other allergens - each 1 (0.1%). In male patients, carba mix, black rubber (PPD) mix and epoxy resin sensitivity was more frequent, whereas nickel sulfate, fragrance mix, ethylenediamine dihydrochloride and cobalt chloride sensitivity was significantly more frequent in female patients. Our results are in general agreement with previously published reports, excluding the low sensitivity rates to cobalt, which maybe is missed by TRUE test ((R)).

Magnusson. B., Blohm. S. G., Fregert, S., Hjorth, N., Hovding, G., Pirilii, V. & Skog, E. (1968). "Routine patch testing IV." *Aeta derm.-vener., Stockh.* **48**, 110. **Cropwatch comments:** Cited by Opdyke (1974) in the RIFM monograph on Peru Balsam regarding studies with 4000 patients patch-tested in five European clinics, 1000 of whom were engaged in domestic work only, including 281 women with contact dermatitis of the hands. Half of the 281 women gave a positive patch test, the commonest allergen being balsam (27%).

Malten, K. E., Frcgert, S., Bandmann, H.-J., Calnan, C. D., Cronin, E., Hjorth, N., Magnusson. B., Maibach, H. I., Meneghini, C. L., Piril-i, V. & Wilkinson, D. S. (1971). "Occupational dermatitis in five European dermatological departments." *Berufsdermatosen* **19**, 1. **Cropwatch comments:** Also cited by Opdyke (1974) in the RIFM monograph on Peru Balsam regarding a collaborative study of contact dermatitis in 5 dermatology depts. using an analysis of the first of the first 4000 patients. Occupational dermatitis was diagnosed in 28% of 1618 men & 13% of the 2382 women. "Peru balsam was equally involved in both occupational and non-occupational groups and may be considered a consumer hazard as well as an occupational one".

Marinovic-Kulisic S., Lipozencic J. & Pastar Z. (2006) "Contact allergy and sociodemographic characteristics." *Coll Antropol.* **30**(2), 273-8. [Abstract](#). The aim of the study was to determine the frequency of positive patch test reaction to different contact allergens according to patients age, sex, occupation and clinical features. Between 1999 and 2003, patch testing was performed in 3,293 patients with respective clinical diagnoses. Patch testing was done by the standard technique proposed by the International Contact Dermatitis Research Group (ICDRG). Study results showed statistically significant differences in patch test response according to sex and age for three allergens (cobalt chloride, nickel sulphate and thiomersal); according to occupation for nine allergens (cobalt chloride, nickel sulphate, balsam of Peru, fragrance mix, thiuram mix, wood tars, neomycin sulphate, thiomersal and detergents), and clinical diagnosis for two allergens (nickel sulphate, and wood tars). The most common and relevant allergens were: nickel sulphate, cobalt chloride and carba mix. They were found in all examinees regardless of age, sex, occupation and diagnoses. The increased awareness of allergens and their potential sources may help to limit the usage of these chemicals in manufacture of consumer products.

Matsuoka Y. & Saito F. (1984) "Three cases of allergic contact dermatitis from spectacle frames." *Hifu (Skin Research)* **27**, 457-461.

Matthies C., Dooms-Goossens A. & Lachapelle J.M., Lahti A., Menne T., White I.R. & Wilkinson J. (1988) "Patch testing with fractionated balsam of Peru." *Contact Dermatitis* **19**, 384-385. **Cropwatch comments:** The authors repeat Hjorth's petroleum ether fractionation studies on Peru balsam with larger numbers of patients, but could not repeat Hjorth's correspondence between the raw Peru balsam and the proposed extract.

Mitchell J.C. (1975) "Patch testing with some components of balsam of Peru." *Contact Dermatitis* **1**, 391-392. [Abstract](#). Some recent publications concerning perfume contact sensitivity are briefly reviewed. Japanese workers have identified some perfume sensitizers and have devised an allergen replacement system. Costus absolute of perfumery has been found to sensitize guinea-pig and man; sesquiterpene lactones are responsible for cross-sensitivity with some other plant products. Balsam of Peru is a useful screen for perfume sensitivity; terpenoids of balsams require study. **Cropwatch comments:** Amongst other matters, the authors pass comment on Nakayama's 1974 paper (Nakayama, H., Hanaoka, H. & Ohshiro, A. (1974) *Allergen controlled system (ACS)*, p42. Tokyo: Kanehara Shuppan) which, on the basis of patch reactions in 183 patients (one positive to Peru Balsam) showed that contact allergy to Peru balsam is rare in Japan.

Mitchell J.C., Calnan C.D., Clendenning W.E. *et al.* (1976) "Patch testing with some components of balsam of Peru" *Contact Dermatitis* **2**, 57-58.

Mögling R. (1880) "Urticaria durch Peru balsam." *Berl Klin Wschr* **17**,557-558, 1880.

Moser E, Bien E. & Jung F. (1968) "Rudas' testing of stimulation of granulation with Peru balsam, salicylaldehyde, methylamino-p-oxyacetophenone, p-tolylmethylcarbinol and phthalic acid-mono-p-tolylmethylcarbinolester" *Acta Biol Med Ger.* **21**(5), 693-6.

Niinimaki A. (1995) "Double-blind placebo-controlled peroral challenges in patients with delayed-type allergy to balsam of Peru." *Contact Dermatitis.* **33**(2), 78-83. [Abstract](#). Patch tests (PTs) with spices, such as clove, cinnamon, Jamaica pepper and vanillin sugar, and with balsam of Peru were made on 29 patients 0.8-2.9 years after an allergy to balsam of Peru had been detected. Positive reactions to balsam of Peru were seen in 17 patients and to clove, Jamaica pepper or cinnamon in 5. Double-blind placebo-controlled peroral challenges (DBPCPCs) with balsam of Peru and spices (active substances) were performed on 22 patients. A substantial increase (30-280%) in the number of palmar vesicles after the DBPCPC with the active substances, but not with placebo, was seen in 8 patients, an increase with both the active substances and placebo in 3, and with placebo but not the active substances in 1 patient. 4 of the 8 patients with positive DBPCPCs with the active substances were negative to balsam of Peru in the 2nd PT. No other objective symptoms were seen after the DBPCPCs. Balsam of Peru and the spices were retested

3 months after the DBPCPC. Both alleviation and aggravation of the PT reactions were seen. It is concluded that ingested flavoured foods might cause systemic contact reactions in some patients with allergy to balsam of Peru, but the benefits of a flavour-avoiding diet are questionable in all of them.

Novak M. & Kviclova E. (1985) "Analysis of the results of epicutaneous tests at the Dermatologic Clinic of the Faculty Hospital in Prague." *Csl Dermatol* **60**, 305-316, 1985

Olholm-Larsen P. & Heydenreich G. (1976) "Allergy to balsam of Peru and wood tars: an increasing problem?" *Contact Dermatitis* **2**(5), 293-4.

Opdyke D.L.J. (1974) "Peru Balsam" *Fd. Cosmet. Toxicol.* **12**, 951-952

Opdyke D.L.J. (1974) "Peru Balsam Oil" *Fd. Cosmet. Toxicol.* **12**, 953-954. **Cropwatch comments:** RIFM tested several samples of PBO - see *FCT* (1974) **12**, p953 -954. The irritation studies were carried out using from two to five numbered samples of PBO (manufacturing methods not stated), not tracked from a botanically verified source, nor batch-tracked by unique identifying code, nor confirmed tested as 100% botanically derived (although the monograph reports that analysis was carried out). As Peru balsam oil is usually a white semi-solid when pure, the material is commonly adulterated by industry to produce a free flowing liquid. **The lack of proper botanical & chemical authentication of the test materials would nowadays ensure the consignment of these studies to the dustbin.** One researcher found that 100% PBO applied to intact or abraded rabbit skin for 24 hr. under occlusion was slightly irritating; however another researcher using a different sample under the same conditions & same animal species found that PBO wasn't irritating. Two different samples of 100% Peru balsam applied to the backs of hairless mice were found non-irritating. Irritation tests on human volunteers using five different 8% Peru balsam oil in a closed patch test produced no irritation in 24 hrs. The sensitization studies were carried out using maximisation tests employing five similarly non-authenticated PBO samples (8% in petroleum) in closed patch tests - **which produced no reactions in 25 human volunteers.** On the basis of these tests, IFRA restricted Peru balsam oil to 0.4% in the final product in 1991 quoting the above RIFM (1974) work – work which, in fact, gives the oil a fairly clean bill of health. There may well have been a good reason for IFRA to restrict use of Peru balsam oil in fragrances, but if there was, they didn't publish the proof at the time.

Oppel T. & Schnuch A. (2006) "The most frequent allergens in contact dermatitis" *Dtsch Med Wochenschr* **131**(28-29),1584-9. **Abstract.** BACKGROUND AND OBJECTIVE: The prevalence of allergic contact dermatitis is high. Patch testing is the standard procedure to detect contact sensitivity. More than 3000 allergens are known, today. On the basis of the data of this study the top allergens are presented. PATIENTS AND METHODS: The retrospective analysis is based on the patch test results collected by the Information Network of Departments of Dermatology in 2004. Data of 9948 patients (6175 female und 3773 male) referred for the evaluation of suspected contact allergy were analysed to determine the frequency of sensitization to the 10 most common contact allergens. RESULTS: The top ten allergens were nickel sulphate (frequency of sensitization standardized for sex and age 17.2 %), fragrance mix (7.2 %), balsam of Peru (6.7 %), cobalt chloride (6.5 %), potassium dichromate (5.3 %), colophony (4.6 %), lanolin alcohol (4.3 %), p-phenylenediamine (4.2 %), ammoniated mercury (3.5 %) und methyldibromoglutaronitrile/phenoxyethanol (3.4 %) in 2004. CONCLUSIONS: Even after healing of the skin lesions of allergic contact dermatitis, it must be considered that sensitization persists indefinitely. Therefore, patients have to be informed exactly about their relevant contact allergens to ensure complete avoidance. To do so, physicians need a detailed knowledge of the most common contact allergens which are discussed in this paper.

Oxholm A., Heidenheim M., Larsen E., *et al.* (1989) "Methyl cinnamate: A newly recognized fraction of balsam of Peru." *Am J Contact Dermatitis* **1**, 43-46.

Panconesi E., Sertoli A., Fabbri P., *et al* (1975) "Computer data on patch tests of 688 eczema patients" *Contact Dermatitis* **1**, 317-318.

Panconesi E., Sertoli A., Spallanzani P. & Giorgini S. (1980) "Balsam of Peru sensitivity from a perfumed cutting fluid in a laser factory." *Contact Dermatitis* **6**(4), 297.

Paschoud J.M. (1967) "In what concentration should Peru balsam be tested?" *Dermatologica* **135**(4), 258-63.

Pfutzner W., Thomas P., Niedermeister A., Pfeiffer C., Sander C., & Przybilla B. (2003) "Systemic contact dermatitis elicited by oral intake of Balsam of Peru" *Acta Derm. Venerol.* **83**(4), 294-5.

Pfutzner W, Niedermeier A, Thomas P. & Przybilla B. (2003) "Systemic contact eczema against Balsam of Peru" *J. Dtsch. Dermatol. Ges.* **1**(9),719-21. **Abstract:** Balsam of Peru (PB; *Myroxylon pereirae*) is a natural product derived from resin of a tropical tree (*Myroxylon balsamum* (L.) Harms var. *pereirae* (Royle) Baillon). Because of its antiseptic and aromatic properties PB or PB-components can be found worldwide not only in many health care and cosmetic products, but also in food items and semi-luxury food. PB contains a wide variety of potent contact allergens leading to hypersensitivity reactions not only after topical application but also oral uptake. We report a 51-year-old brewer with chronic eczema of the hands who showed delayed-type patch test reactions against PB and fragrance-mix. Oral PB-challenge led to exacerbation of the eczema 5 and in a repeated test 2 days later. We here review this probably quite often overlooked disease and the therapeutic consequences which require profound knowledge about the wide distribution of PB when advising the patient about a PB-restricted diet. In addition, this unusual case report demonstrates that one has to consider marked delayed hypersensitivity reaction when investigating a systemic contact allergy.

Reinitzer F (1914) "Untersuchungen fiber Siam-Benzoe." *Arch Pharm* **252**, 341-349.

Reinitzer F (1925) "Untersuchungen tiber Siam-Benzoe." *Arch Pharm* **263**, 347-358, 1925.

RIFM (Research Institute for Fragrance Materials, Inc.), 2004. Local Lymph Node Assay on Peru balsam (*Myroxylon pereirae* Klotzsch). RIFM report number 44372, February 16 (RIFM, Woodcliff Lake, NJ, USA). **Cropwatch comments:** believed not to available within the public domain

RIFM (Research Institute for Fragrance Materials, Inc.), 2005. Repeated insult patch test with balsam, Peru (*Myroxylon pereirae* Klotzsch). RIFM report number 47380, January 20 (RIFM, Woodcliff Lake, NJ, USA). **Cropwatch comments:** believed not to available within the public domain

RIFM (Research Institute for Fragrance Materials, Inc.), 2004. Local Lymph Node Assay on Peru balsam absolute. RIFM report number 44371, February 16 (RIFM, Woodcliff Lake, NJ, USA). **Cropwatch comments:** believed not to available within the public domain

Le Roy R., Grosshans E. & Fousereau J. (1981) "[Investigation of contact allergies in 100 cases of ulcus cruris (author's transl)]" *Derm Beruf Umwelt.* **29**(6), 168-70. **Abstract.** In a group of 100 patients with ulcus cruris, the incidence of contact allergies was determined. Patch tests were applied with 18 products that might have come into contact with the skin. These products comprised drugs and excipients (preservatives and ointment vehicles) potential ingredients of tapes or of elastic bandages. Peru balsam (14%), wool-wax alcohols (10%), Nestosyl owing to its para-aminobenzoate component (7%), neomycin (5%) and Thyme oil (5%) were the allergens most frequently encountered.

Rudzki E. & Kleniewska D. (1971) "Kontaktallergie auf einige Lokalthérapeutika und Konservierungsmittel." *Dermatologica* **143**, 36-42.

Rudzki E. & Kielaz D. (1972) "Sensitivity to some compounds related to balsam of Peru." *Contact Dermatitis Newslett* **12**, 335.

Rudzki E. & Grzywa Z. (1976) "Immediate reactions to balsam of Peru, cassia oil and ethyl vanillin." *Contact Dermatitis* 2(6), 360-1.

Rudzki E. & Grzywa Z. (1977) "Balsam of Peru as screening agent for essential oils sensitivity." *Dermatologica* 155(2), 115-21. [Abstract](#). The standard series and 35 essential oils were tested on 450 patients with dermatitis. It was found that those simultaneously sensitive to essential oils are more frequently negative than positive to balsam of Peru. The remaining 3 balsams, however (colophony, turpentine and wood tars), are also screening agents for essential oils. All four balsams reveal sensitivity to essential oils in most of the subjects tested. In patients negative to all 4 balsams of the standard series, attempts to find an essential oil with which tests would be simultaneously frequently positive with those for other essential oils failed.

Rudzki E. & Rebandel P. (2006) "100 patients positive to balsam of Peru observed in Warsaw (Poland)." *Contact Dermatitis*. 55(4), 255. [Abstract](#). From 15 March 2003 to 31 December 2005 in 2247 consecutive patients with dermatitis (788 men and 1459 women), we observed 100 patch-tested persons (39 men and 61 women) positive to balsam of Peru (*Myroxylon pereirae* resin, MP). In all submitted to patch tests, 4.45% (4.95% men and 4.18% women) were sensitive to balsam of Peru (in 2003: all patients 4.01%, men 3.92%, and women 4.00%; in 2004: all patients 4.15%, men 5.00%, and women 3.97%; and in 2005: all patients 4.96%, men 5.39%, and women 4.73%). For comparison in 1994, the same incidence was 2.82% in all tested, 2.84% in men, and 2.81% in women, and in 1995, the incidence was 3.56% in all patients, 3.67% in men, and 3.44% in women (over the past years, there is an increase in the prevalence of the sensitization to MP) In a group of 100 patients recently positive to MP, 49 patients (51.13% men and 47.54% women) were older than 60 years and 13 persons (10.26% men and 14.75% women) were younger than the 30 years. Among 100 patients positive to balsam, 38 were also positive to perfume mixture (38.46% men and 37.71% women), 18 to colophony (10.26% men and 22.95% women), but no one to turpentine. Positive response only to MP was found in 32 persons (13 men and 19 women). Some data (also relevance) were not available for all 100 patients. In our other study (1) of 300 patients with stasis dermatitis (out of 1418 consecutive patients with dermatitis) 30.00% were sensitive to MP. We agree with supposition that the sensitization to balsam of Peru is due not only to the use of cosmetics but also of topical medicaments

Salam T.N. & Fowler J.F. (2001) "Balsam-related systemic contact dermatitis." *J. Am. Acad.* 45(3) 470-2. [Abstract](#). BACKGROUND: Positive patch tests to balsam of Peru (BOP) or fragrance mix (FM) suggest the possibility of systemic contact dermatitis from balsam-related foods and spices. OBJECTIVE: This was a retrospective study to determine whether avoidance of balsam-related foods results in an improvement of dermatitis in these patients. METHODS: A review of the records of all patients seen from July 1 to Dec 31, 1998 with positive patch tests to BOP, FM, cinnamic aldehyde, and balsam of tolu was performed 9 to 14 months after their evaluation in a tertiary dermatology center. All patients were contacted via telephone to assess the status of their dermatitis and whether they were able to note any specific balsam-related food allergies. RESULTS: A total of 75 patients were identified, and 71 could be contacted. Fourteen were only allergic to BOP or FM on testing; 31 were positive to BOP/FM and other allergens with presumed relevance to BOP/FM; 26 were positive to BOP/FM and others with other allergens felt to be responsible for the dermatitis and were not placed on a BOP diet. Excluding this last group, 21 of 45 (47%) had complete or significant improvement that they related to dietary modification. Ten did not modify their diet, with 8 reporting no improvement. Eight improved with fragrance or other allergen avoidance only, and 6 modified their diet unsuccessfully. Most commonly implicated foods included tomatoes, citrus, and spices. CONCLUSION: Almost half of the subjects with positive patch tests to BOP or FM who followed a BOP reduction diet reported significant to complete improvement of their dermatitis.

Schafer T., Heinrich J., Bohler E., Klemm E., Merkl J., Ruhdorfer S., Weigl L., Wessner D., Wichmann H.E., Ring J & MONICA/KORA-Studiengruppe.(2005) "Allergies in adults" *Gesundheitswesen* 67 (Suppl 1), S187-92. [Abstract](#). Only few epidemiological studies have assessed allergic diseases in adults. In a follow-up study of the MONICA survey S3 (1994/95),

which was performed 1997-1999, a total of 1,537 persons were interviewed and tested by skin prick and patch test. Furthermore data of the MONICA survey (RAST, cholesterol, food diaries) could be used. Within survey S4 (1999/2001) a total of 4,261 subjects were interviewed concerning their personal history of atopic diseases and the corresponding history of their partners. In survey S3 the prevalence of allergic sensitisation was 20.5 % for persons without formal graduation from school and 48.1 % for those with a university degree. 20.8 % reported a hypersensitivity to food and about one quarter exhibited a positive reaction in skin prick test. Atopic eczema and hay fever increased over quartiles of HDL cholesterol. Similar, allergic sensitisation (RAST) increased over quartiles of uptake of unsaturated fatty acids in men. 40 % of those who were patch tested exhibited a positive reaction, with perfume mix, nickel, thimerosal and balsam of Peru being the most prominent allergens. Inhabitants of the City of Augsburg were sensitised more often (34.0 % overall, 23.9 % pollen) than inhabitants of villages with (29.4 %, 17.0 %). Full time farmers were sensitised less frequently (22.0 %, 8.4 %). In survey S4 the lifetime prevalence of atopic diseases diagnosed by doctors was 5.1 % for atopic eczema, 6.1 % for asthma and 13.7 % for hay fever. Subjects who lived together with a partner who suffered from hay fever were affected in 19.6 % whereas 13.1 % had hay fever when the partner was not affected. Future studies will offer an unique opportunity to analyse the incidence and remission of manifestations of atopy in adults.

Schnuch A., Lessman H., Geier J., Frosch P.J., Uter W. & IVDK. (2004) "Contact Allergy to Fragrances: frequencies of sensitisation from 1996 to 2002. Results of the IVDK." *Contact Derm.* **50**(2), 65-76. [Abstract](#). Increasing frequencies of sensitization to the fragrance mix (FM) have been acknowledged as a serious problem for many years. It is well known that the single compounds (SCs) of the FM contribute differently to the FM patch test reactions. In this study, we were interested in the time trends of the FM, the SCs, *Myroxylon pereirae* resin (MP; balsam of Peru) and oil of turpentine (OT) as possible further indicators of perfume allergy and analysed the data collected by the Information Network of Departments of Dermatology multicentre project from 1996 to 2002. During the study period (1996–2002), the FM [8% petrolatum (pet.)], MP (25% pet.) and OT (1% pet.) were tested in 59 298, 59 334 and 59 478 patients, respectively. SCs were tested in a selected group of patients, ranging from n¼1083 to n¼1924 per year. A significant increase in the proportions of patients with positive reactions to FM, MP and OT between 1996 and 1998 is noted, and a significant decline from 1999 to 2002 (Cochrane Armitage trend test, P<0.0001). The highest frequency of sensitization to the FM was 13.1% in 1999, and the lowest 7.8% in 2002. The number of concomitant reactions to OT, a surrogate marker for terpenes, in FM-positive patients was significantly increased between 1997 and 1999. Reactions to SCs in FM-positive patients were observed in 29.9% (oak moss absolute) to 5.9% (geraniol). There was no time trend in reactions to SCs, although the relative share was increased for isoeugenol, cinnamic aldehyde and geraniol in 1999. In summary, we report for the first time, a significant decline in sensitization to the FM, very probably due to a reduced exposure (less potent allergens used in fine fragrances, possibly less use of natural ingredient-based cosmetics and lowered use concentration of important fragrance allergens). The differences in ranking of SCs could stimulate (a) a redefinition of the FM and (b) a differentiated preventive and regulatory approach, with oak moss and isoeugenol being regulated strictly by prohibition, concentration limits further reconsidered and/or health warnings and clearly less noxious substances like geraniol treated less restrictively.

Swoboda B. & Ludvan M. (1973) "Zum ~ Alergiespektrum bei Unterschenkelelkzemen." *Z. Hautkr* **49**, 149-155.

Tanaka S., Matsumoto Y., Dlova N., Ostlere L.S., Goldsmith P.C., Rycroft R.J., Basketter D.A., White I.R., Banjeree P., McFadden J.P. (2004) "Immediate contact reactions to fragrance mix constituents and *Myroxylon pereirae* resin." *Contact Derm.* **51**(1), 20-1. [Abstract](#). We have studied patients who have positive-patch test reactions to fragrance-allergic screening substances fragrance mix (FM) or *Myroxylon pereirae* resin (balsam of Peru) for immediate contact reactions to the standard FM, the constituents of the FM and *Myroxylon pereirae* resin. In the fragrance-positive subjects (n = 60), there were positive immediate contact reactions to

*Myroxylon pereirae* resin in 56.6% and to FM in 11.6%. In a control group (n = 50) of eczematous, patch test-negative patients there were positive immediate reactions to *Myroxylon pereirae* resin in 58.0% subjects and to FM in 12.0%. The absence of a significant difference between the fragrance-allergic group and control group is in keeping with a non-immunological basis for the majority of the immediate reactions seen.

Telang G.H. & Brod B.A. (1994) "Allergic contact dermatitis to eyeglass frame nosepieces." *J. Am. Acad. Dermatol* **31**, 114-115.

Temesvari E., Soos G., Podanyi B., Kovacs I. & Nemeth I. (1977) "Peru balsam contact urticaria" *Orv Hetil.* **118**(30), 1767-8.

Temesvari E., Soos G., Podanyi E., Kovacs I. & Nemeth I. (1978) "Contact urticaria caused by Peru balsam." *Derm Beruf Umwelt.* **26**(3), 81-2. [Abstract](#). By tests on six patients with recurrent urticaria it could be demonstrated that it was caused by an allergy against Peru balsam. Different reaction types seem to have been responsible for the occurrence of the urticaria. Cross reactions with different other substances, mainly luxury food and stimulants, play a particular part

Temesvári E., Soos G., Podányi B., Kovács I. & Nemeth I. (1978) "Contact urticaria provoked by Balsam of Peru." *Contact Derm.* **4**, 65-68. [Abstract](#). Six patients with chronic urticaria are described in whom immediate type hypersensitivity to balsam of Peru was proven by patch test.

Thune P. (1981) "Photosensitivity & allergy to cosmetics." *Contact Dermatitis* **7**(1), 54.

Trattner A. & David M. (2003) "Patch testing with fine fragrances: comparison with fragrance mix, balsam of Peru and a fragrance series" *Contact Derm.* **49**(6), 287-9. [Abstract](#). High frequencies of contact allergy to fragrance ingredients have been reported in recent years. Only approximately 70-80% are detected by fragrance allergens in the standard patch test series. This investigation compares the patch test reactions to fine fragrances with reactions to fragrance mix (FM), balsam of Peru (BP) (*Myroxylon pereirae* resin) and a fragrance series. 641 consecutive patients with eczema were patch tested with the European standard series and with selected fine fragrances. Those who were positive to 1 of the fine fragrances or the FM or BP were also tested with the fragrance series. 95 (14.8%) patients were found to have a positive patch test reaction to FM or BP; 41 (6.4%) had positive results to fragrance no. 1 and 29 (4.5%) to no. 2. 9 (9.5% of the 95 positive patients) had a positive reaction to fine fragrances and a negative reaction to all other fragrance allergens in the standard series. These findings indicate that testing with fine fragrances can add to our evaluation of fragrance-sensitive patients.

Tschirch A, Trog H (1894) "Untersuchungen u"ber die Secrete. 7. Studien u"ber den Perubalsam und seine Entstehung." *Arch Pharmazie* **232**, 70-98.

Tschirch A. & Stock E. (1935) *Die Harze*. Berlin: Gebrüder Bornträger, Vol 2, 1935

Uter W., Hegewald J., Aberer W., Ayala F., Bircher A.J., Brasch J., Coenraads P.J., Schuttelaar M.L., Elsner P., Fartasch M., Mahler V., Belloni Fortina A., Frosch P.J., Fuchs T., Johansen J.D., Menne T., Jolanki R., Krecisz B., Kiec-Swierczynska M., Larese F., Orton D., Peserico A., Rantanen T. & Schnuch A. (2005) "The European standard series in 9 European countries, 2002/2003 -- first results of the European Surveillance System on Contact Allergies." *Contact Dermatitis* **53**(3), 136-45 [Abstract](#). Since January 2001, the European Surveillance System on Contact Allergies (ESSCA), supported by European Union funding (contract QLK4-CT-2001-00343), has started to collect patch-test data. This comprises a standardized clinical history and the patch-test results using the European standard series, from 17 centres in 9 European countries listed above. In 2002 and 2003, 10 511 patients' test results have been pooled and analysed. The anamnestic data partly reflect the subspecialties of some centres. The most common allergen was nickel sulfate (17.3%); however, large international variations were observed. The prevalence of contact allergy to *Myroxylon pereirae* resin (balsam of Peru) (5.8%) is coming close to the frequency found with the fragrance mix (6.4%). Regarding contact allergy to chromium compounds, different frequencies were noted in the 2 centres focused on

occupational dermatitis (2.3% in the FIOH versus 7.4% in the Nofer Institute). These most likely reflect the beneficial effect of addition of ferrous sulfate in one, but not the other country. As differences may partly be due to different patch-test reading, standardization may need to be refined further. By providing post-marketing surveillance in the field of contact allergy, ESSCA will meet its objective of increased consumer safety across Europe.

Veien N.K., Hattel T., Justesen O. & Norholm A (1983) "Oral challenge with balsam of Peru in patients with eczema: a preliminary study." *Contact Dermatitis*. **9**, 75-76.

Veien N.K., Hattel T., Justesen O. & Norholm A. (1985) "Reduction of intake of balsams in patients sensitive to balsam of Peru." *Contact Dermatitis* **12**(5), 270-3. [Abstract](#). 64 patients participated in this study. 24 were patients who had positive patch tests to balsam of Peru. The dermatitis of 9 of the patients had flared after open oral challenge with balsam of Peru, and the dermatitis of 31 patients had flared after double-blind oral challenge. All 64 patients were asked to avoid food items suspected of containing balsams for 1 to 2 months. At the end of that time, an evaluation of the diet trial was made; the dermatitis of 37 had cleared or improved markedly. If an improvement had taken place, the patient was asked to continue to diet moderately. 6 months to 3 years after the diet was initiated, a questionnaire was mailed to those patients whose dermatitis had improved after the first trial. The patients were asked to evaluate the long-term benefit of following the diet. 30 felt there was a long-term effect, and 27 still followed the diet instructions to some degree.

Veien N.K., Hattel T., Justesen O. & Norholm A. (1985) "Oral challenge with balsam of Peru." *Contact Derm.* **12**, 104-107. [Abstract](#). A placebo-controlled, double-blind, oral challenge with balsam of Peru was carried out in 221 patients with various types of dermatitis. 210 patients completed the study, and 45 of them experienced a flare of their symptoms after challenge with balsam of Peru but not after placebo. 15 patients reacted to the placebo, and 5 reacted to both balsam and placebo. Specific reactivity to balsam of Peru was seen particularly in patients with positive patch tests to this compound and in some patch-test-negative patients with vesicular hand eczema, ano-genital and axillary eczema. Dietary restriction of the intake of balsams was followed by marked improvement or clearance of the dermatitis in approximately half of the patients who adhered to the diet for at least 1 month.

Veien N.K., Hattel T. & Laurberg G. (1996) "Can oral challenge with balsam of Peru predict possible benefit from a low-balsam diet?" *Am J. Contact Derm.* **7**(2), 84-87. [Abstract](#)  
BACKGROUND: Previous studies have shown that some patients sensitive to balsams and/or fragrances obtain long-term benefits by following a low-balsam diet, whereas others do not. OBJECTIVE: This study was performed to determine whether a low-balsam diet was a helpful long-term treatment for selected patients sensitive to balsam of Peru and/or a perfume mixture and to determine whether oral challenge with balsam of Peru could predict which balsam-sensitive patients might benefit from a reduction in balsam intake. METHODS: Questionnaires were sent to 46 patients with positive patch test results to balsam of Peru and/or a perfume mixture and chronic dermatitis of a morphology consistent with endogenous dermatitis who had experienced improvement after 1 to 2 months on a diet intended to reduce the intake of balsams. The questionnaires were mailed 1 to 3 years after the initiation of the diet treatment to inquire about a possible long-term benefit of the diet. RESULTS: Twenty-eight of the 46 patients stated in the questionnaire that they had long-term benefits from the diet treatment. These included 16 of 22 patients who had reacted to a placebo-controlled oral challenge with 1 g balsam of Peru, 3 of 10 who had no reaction or a placebo reaction to the oral challenge, and 9 of 14 who had not been challenged orally. The efficacy of the diet treatment was not correlated to whether the patient had patch test reactivity to either balsam of Peru, the perfume mixture, or both substances. Food items most commonly mentioned by patients as causing aggravation of their symptoms on at least three different occasions were wine, candy, chocolate, cinnamon, curry, citrus fruit, and flavorings. CONCLUSIONS: In its present form, the oral challenge procedure with balsam of Peru offers only limited assistance in selecting patients who are likely to benefit from diet treatment.

Weston W.L. & Weston J.A. (1984) "Allergic contact dermatitis in children." *Am. J. Dis. Child.* **138**, 932-936.

Wetter D.A., Davis M.D., Yiannias J.A., Cheng J.F., Connolly S.M., el-Azhary R.A., Farmer S.A., Fett D.D., Johnson J.S., Linehan D.L., Richardson D.M., Schroeter A.L. (2005). "Patch test results from the Mayo Clinic Contact Dermatitis Group, 1998-2000." *J Am Acad Dermatol* **53**(3),416-21. [Abstract](#). BACKGROUND: Patch testing is a diagnostic tool for the evaluation of patients with suspected allergic contact dermatitis. A standard series of allergens similar to that used by the North American Contact Dermatitis Group (NACDG) is used at Mayo Clinic. OBJECTIVE: Our aim was to report the results of patch testing with a standard series at Mayo Clinic from July 1, 1998, to Dec 31, 2000 and to compare our findings with those of the NACDG during the same period. METHODS: The results of patch testing with the standard series at Mayo Clinic were examined. Positive reaction rates were compared between Mayo Clinic and the NACDG. RESULTS: During the 30-month period, 1324 Mayo Clinic patients were patch tested with a standard series of allergens (mean, 60 allergens), whereas the NACDG standard series during this period included 50 allergens. Overall, 917 patients (69.3%) had at least one positive reaction and 606 patients (45.8%) had two or more positive reactions. The 10 allergens used both by Mayo Clinic and by the NACDG that most frequently caused positive reactions were nickel sulfate hexahydrate, balsam of Peru (*Myroxylon pereirae*), neomycin sulfate, cobalt chloride, fragrance mix, potassium dichromate (0.25%), thimerosal, bacitracin, formaldehyde, and glutaraldehyde. Statistically significant differences in positive reaction rates ( $P < .05$ ) were observed for 12 of the 43 allergens common to both Mayo Clinic and the NACDG. CONCLUSION: With large standard patch test series, one can identify commonly encountered and potentially relevant contact allergens.

Wohrl S., Hemmer W., Focke M., Gotz M. & Jarisch R. (2001) "The significance of fragrance mix, balsam of Peru, colophony and propolis as screening tools in the detection of fragrance allergy." *Br J Dermatol.* **145**(2), 268-73. [Abstract](#). BACKGROUND: Patch testing to fragrances is an important step in the diagnosis of fragrance allergy. OBJECTIVES: To determine the usefulness of adding propolis to the European standard series to test for fragrance allergy. PATIENTS AND METHODS: A total of 2660 consecutive patients were patch tested with a standard patch test series; 747 suspected of fragrance allergy were tested further with a special fragrance series. RESULTS: The positive results to the standard series in 2660 patients were: fragrance mix 243 (9.1%), *Myroxylon pereirae* [balsam of Peru] 144 (5.4%), colophony 32 (1.2%); these fragrance mixtures are used as screening substances for fragrance allergy in the European standard series. Propolis, also known as bee's glue, was also an important allergen in this locally revised standard series ( $n = 35$ , 1.3%). Positive reactions to the aforementioned allergens were associated significantly among each other ( $P < 0.01$ , chi<sup>2</sup>-test) and did not differ between the sexes. The primary locations of dermatitis in patients with a positive test to one or more fragrance allergens ( $n = 162$ ) among those suspected of fragrance allergy ( $n = 747$ ) were: face 46.9%, hands 23.5%, neck 17.9%, axillae 12.3%; 92 of the 747 patients suspected of fragrance allergy had positive skin tests to the special fragrance series comprising the eight constituents of the fragrance mix (most frequent: isoeugenol 5.4%, oakmoss absolute 5.0%, eugenol 2.5%) and 14 other fragrance allergens (most frequent: clove oil 1.6%, lemon grass oil 0.8%, cedar wood oil 0.7%). The additional value of propolis as another screening substance for fragrance allergy in these patients was low. The likelihood of a reaction to one or more of the extra fragrance allergens increased with the number of reactions to fragrance screening allergens in the standard series. CONCLUSIONS: The number of positive reactions to fragrance screening allergens in a standard patch test series may be used as a rule of thumb for predicting a positive outcome of a more detailed testing to fragrances. Propolis is an important allergen in its own right but its value as a screening substance for fragrance allergy is limited.

### ***Peru Balsam-Related Articles.***

Calnan C.D. (1976) "Cinnamon dermatitis from an ointment" *Contact Dermatitis* **2**(3), 176. [Abstract](#). Six patients are reported who had an allergic contact dermatitis from the use of H proprietary antiseptic ointment containing oil of cinnamon. Three were positive and three negative

to balsam of Peru; two of these and one other also reacted to cinnamic aldehyde. The history and usage of cinnamon is briefly reviewed.

Diepgen T. & Coernraads P.J. (2000) "Sensitivity, Specificity & Positive Predictive Value of Patch Testing: the More you Test, the More you Get?" *Contact Dermatitis* **42**, 315-317.

Fisher A.A. (1975) "Allergic paraben and benzyl alcohol hypersensitivity relationship of the "delayed" and "immediate" varieties" *Contact Dermatitis* **1**(5), 281. **Cropwatch comments:** The author remarks on cross-sensitization to benzyl alcohol having been reported in subjects sensitized to Peru balsam by Hjorth (1961)]. **Abstract.** From a review of the literature, and the results of scratch, intracutaneous and subcutaneous injections of patients with parabens and benzyl alcohol sensitivity of the delayed type characterised by allergic contact dermatitis and strongly positive patch tests, it would appear that such sensitivity is not usually accompanied by the immediate urticarial type of allergic sensitivity. This communication concerns itself with results of testing patients with clinical sensitivity and positive patch test reactions to the parabens or benzyl alcohol with scratch, intracutaneous and subcutaneous injections of these preservatives in order to determine the relationship of the "delayed" type of allergic hypersensitivity to the parabens and benzyl alcohol with the "immediate" variety of hypersensitivity. The parabens and benzyl alcohol are widely employed as preservatives for many allergenic extracts used in scratch and intracutaneous testing. In addition, these preservatives are used in injectable corticosteroid medicaments and in local anesthetic solutions. In order to determine whether the presence of these preservatives in allergenic extracts would produce false positive scratch or intracutaneous tests or might produce an immediate, urticarial or anaphylactic reaction in patients with allergic contact dermatitis and positive patch test reactions to these preservatives, two patients with positive patch test reactions and allergic contact dermatitis to the parabens and two with similar benzyl alcohol sensitivity were tested in the manner detailed in the following case reports.

Khanna M., Qasem K. & Sasseville D. (2000) "Allergic contact dermatitis to tea tree oil with erythema multiforme-like id reaction." *Am J Contact Dermat.* **11**(4), 238-42. **Abstract.** The commercial production of tea tree oil, extracted from *Melaleuca alternifolia* Cheel, has considerably increased over the past 15 years in response to a strong demand for natural remedies and aromatic substances. The number of case reports that describe allergic contact dermatitis (ACD) to this essential oil is also on the rise. We report an additional case of ACD to tea tree oil that presented with an extensive erythema multiforme-like reaction. A skin biopsy was performed from a targetlike lesion distant from the site of the initial dermatitis. The patient was treated with systemic and topical corticosteroids. Five months later, he was patch tested to the North American standard series, to his own tea tree oil, to a fresh batch of tea tree oil, and to some related allergens. The skin biopsy showed a spongiotic dermatitis without histological features of erythema multiforme. Patch testing elicited a 3+ reaction to old, oxidized tea tree oil, a 2+ reaction to fresh tea tree oil, a 2+ reaction to colophony, a 1+ reaction to abitol, and a 1+ reaction to balsam of Peru. We believe this is the first report of erythema multiforme-like reaction secondary to ACD from tea tree oil. Other interesting features are the stronger reaction to oxidized than to fresh tea tree oil, and concomitant reactivity to colophony, abitol, and balsam of Peru.

Matura M., Goossens A., Bordalo O., Garcia-Bravo B., Magnusson K., Wrangsjö K. & Karlberg A.T. (2002) "Oxidized citrus oil (R-limonene): a frequent skin sensitizer in Europe." *J Am Acad Dermatol.* **47**(5), 709-14. **Abstract.** BACKGROUND: Peel oil from citrus fruits consists of R-(+)-limonene, which is one of the most commonly used fragrance materials in technical products and in fine fragrances. This substance forms allergenic oxidation products during handling and storage. OBJECTIVE: We wanted to study the frequency of allergic reactions to oxidized R-(+)-limonene in patients with dermatitis and find a suitable test preparation. METHOD: Patch testing with oxidized R-(+)-limonene was performed on 2273 patients at 4 dermatology clinics in Europe. RESULTS: Of the consecutive patients tested, 3.8% to 3.9% had positive reactions in two of the clinics; 6.5% had positive reactions in the third clinic; and 0.3% had positive reactions in the fourth clinic. A total of 63 patients showed positive reactions. In total, 57% of the patients did not react to fragrance mix or balsam of Peru. We recommend testing with 3% oxidized R-(+)-

limonene in patients referred for patch testing. CONCLUSION: The high frequency of oxidized limonene allergy provides clinical evidence for the European classification of R-(+)-limonene that contains oxidation products as skin sensitizers.

Niinimäki A. (1984) "Delayed-type allergy to spices". *Contact Dermatitis*. **11**(1), 34-40. [Abstract](#). 9 common spices were tested epicutaneously in 338 dermatological patients, 118 of whom were allergic to balsam of Peru. Positive reactions to one or more spices were seen in 50 patients all of whom except 2 were allergic to balsam of Peru. The spices giving positive reactions most often were clove, Jamaica pepper and cinnamon (cassia). 2/3 of the patients allergic to balsam of Peru or spices were women, usually suffering from hand eczema. Peroral challenge with spices was carried out in 71 patients allergic to balsam of Peru. Pompholyx on the palms and other objective symptoms were encountered in 7 cases, 3 of whom showed no reactions to spices in epicutaneous tests.

Scardamaglia L., Nixon R. & Fewings J. (2003) "Compound tincture of benzoin: A common contact allergen?" *Australasian Journal of Dermatology* **44**(3), 180. [Abstract](#). SUMMARY. The results of patch testing to compound tincture of benzoin in 477 patients performed at the Contact Dermatitis Clinic at the Skin and Cancer Foundation in Melbourne during 1999 are presented. There have been fewer than 30 reported cases of contact allergy from compound tincture of benzoin, and none in the last decade. Our results showed 45 out of the 477 patients had a positive reaction to compound tincture of benzoin, which was the third most common allergen in our series. Of these 45 patients, 14 had strong positive reactions, but only two definitely recalled exposure to compound tincture of benzoin and these were clinically relevant. Twenty-eight of these patients had cross-reactions to similar allergens (fragrance mix, balsam of Peru, colophony and tea tree oil). Of the 14 patients with a strong positive reaction to compound tincture of benzoin, 11 had at least one other positive cross-reaction to the above allergens. This may explain the high frequency of reaction to compound tincture of benzoin found in our study.

Schubert H.J. (2006) "Skin diseases in workers at a perfume factory." *Contact Dermatitis* **55**(2), 81-3. [Abstract](#). The aim of this study is to find out the causes of skin diseases in one-third of the staff of a perfume factory, in which 10 different perfume sprays were being manufactured. Site inspection, dermatological examination and patch testing of all 26 persons at risk with 4 perfume oils and 30 ingredients of them. The results showed 6 bottlers were found suffering from allergic contact dermatitis, 2 from irritant contact dermatitis, 12 workers showed different strong reactions to various fragrances. The main causes of allergic contact dermatitis were 2 perfume oils (12 cases) and their ingredients geraniol (12 cases), benzaldehyde (9), cinnamic aldehyde (6), linalool, neroli oil, terpenes of lemon oil and orange oil (4 each). Nobody was tested positive to balsam of Peru. Job changes for office workers, packers or printers to other rooms, where they had no longer contact with fragrances, led to a settling. To conclude, automation and replacement of glass bottles by cartridges from non-fragile materials and using gloves may minimize the risk.

## Towards a Selective Propolis Bibliography.

Alencar S.M., Oldoni T.L., Castro M.L., Cabral I.S., Costa-Neto C.M., Cury J.A., Rosalen P.L., Ikegaki M. (2007) "Chemical composition and biological activity of a new type of Brazilian propolis: red propolis." *J Ethnopharmacol*. **113**(2):278-83. [Abstract](#). Propolis has been used as a medicinal agent to treat infections and promote wound healing for centuries. The aim of the present study was to test the antimicrobial, antioxidant, and cytotoxic activities of a new type of Brazilian propolis, popularly called red propolis, as well as to analyze its chemical composition. The antimicrobial activity against *Staphylococcus aureus* ATCC 25923 and *Staphylococcus mutans* UA159 was evaluated and the chloroform fraction (Chlo-fr) was the most active with lower MIC ranging from 25 to 50 microg/ml. The hexane fraction (H-fr), having the highest concentration of total flavonoids, showed the best sequestering activity for the free radical DPPH. The ethanolic

extract of propolis (EEP) showed cytotoxic activity for the HeLa tumor cells with an IC(50) of 7.45 microg/ml. When the EEP was analyzed by GC-MS, seven new compounds were found, among which four were isoflavones. Our results showed that the red propolis has biologically active compounds that had never been reported in other types of Brazilian propolis.

Arvouet-Grand A., Lejeune B., Bastide P., Pourrat A., Privat A.M. & Legret P. (1993) "[Propolis extract. II. Wound healing the rat and rabbit]" *J. Pharm Belg.* **48**(3), 171-8. [Abstract](#). This work is related to wounds healing properties of a propolis extract. In first study on the Albinos Rabbit, the activity of a propolis extract is compared with these of a Peru balsam. Optimal concentrations of them in ointments are evaluated by applications on deep cutaneous scarifications. In order to go further into details, we have chosen in second part, another assay on the Rat, allowing the obtention of deeper wounds; By this way, more complete quantification of retained parameters and a better appraising of the wounds healing process evolution are possible.

Bankova V., De Castro S.L. & Marcucci M.C. (2000) "Propolis: recent advances in chemistry and plant origin." *Apidologie* **31**, 3–15.

Bankova V., Boudourova-Krasteva G., Popov S., Sforcin J.M. & Funari S.R.C. (1999) "Seasonal variations in essential oil from Brazilian propolis." *J. Essent. Oil Res.* **10**, 693-6.

Bankova V., Boudourova-Krasteva G., Popov S., Sforcin J.M., Funari S.R.C. (1999) "Seasonal variations of the chemical composition of Brazilian propolis." *Apidologie* **29**, 361-7.

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Banskota A., Tezuka Y., Midorikawa K., Matsushigem K. & Kadota Sh. (2000) "Two novel cytotoxic benzofuran derivatives from Brazilian propolis," *J. Nat. Prod.* **63**, 1277–1279.

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Downs A.M. & Sansom J.E. (1998) "Occupational contact dermatitis due to propolis." *Contact Dermatitis* **38**, 359-360.

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Ghisalberti E.L. (1979) "Propolis: a review." *Bee World* **60**, 59-84

Grundberger D., Banerjee R., Eisinger K., Oltz E.M., Efros L., Caldwell M., Estevez V., Nakanishi K. (1988) "Preferential cytotoxicity on tumor cells by caffeic acid phenethyl ester isolated from propolis." *Experientia* **44**, 230–232.

Hausen B.M., Wollenweber E., Senff H. & Rost B. (1987) "Propolis allergy (I). Origin, properties, usage and literature review." *Contact Dermatitis* **17**, 163-170.

Hausen B.M., Wollenweber E, Senff & Post B. " Propolis allergy (II). (1987) "The sensitizing properties of 1,1-dimethylallyl caffeic acid ester." *Contact Dermatitis* **17**, 171–177.

Hausen B.M. & Wollenweber E. (1988) "Propolis allergy (III). Sensitization studies with minor constituents." *Contact Dermatitis* **19**, 296–303.

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Hirota M., Matsuno T., Fujiwara T., Sugiyama H., Mineshita S. (2000) "Enhanced cytotoxicity in a Z-photoisomer of a benzopyran derivative of propolis." *J. Nat. Prod.* **63**, 366–370.

Li F., Awale S., Tezuka Y. & Kadota S. (2008) "Cytotoxic constituents from Brazilian red propolis and their structure-activity relationship." *Bioorg Med Chem.* 2008 Apr 12. [Abstract](#). Several classes of flavonoids [flavanoids (1-10), flavonol (11), isoflavones (12-18), isoflavanones (19-22), isoflavans (23-26), chalcones (27-30), auronol (31), pterocarpan (32-37), 2-arylbenzofuran (38), and neoflavonoid (39)] and lignans (40-42) isolated from the MeOH extract of Brazilian red propolis were investigated for their cytotoxic activity against a panel of six different cancer cell lines including murine colon 26-L5 carcinoma, murine B16-BL6 melanoma, murine Lewis lung carcinoma, human lung A549 adenocarcinoma, human cervix HeLa adenocarcinoma, and human HT-1080 fibrosarcoma cell lines. Based on the observed results, structure-activity relationships were discussed. Among the tested compounds, 7-hydroxy-6-methoxyflavanone (3) exhibited the most potent activity against B16-BL6 (IC<sub>50</sub>, 6.66μM), LLC (IC<sub>50</sub>, 9.29μM), A549 (IC<sub>50</sub>, 8.63μM), and HT-1080 (IC<sub>50</sub>, 7.94μM) cancer cell lines, and mucronulatol (26) against LLC (IC<sub>50</sub>, 8.38μM) and A549 (IC<sub>50</sub>, 9.9μM) cancer cell lines. These activity data were comparable to those of the clinically used anticancer drugs, 5-fluorouracil and doxorubicin, against the tested cell lines, suggesting that 3 and 26 are the good candidates for future anticancer drug development.

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Magro-Filho O. & de Carvalho A C. (1994) "Topical effect of propolis in the repair of sulcoplasties by the modified Kazanjian technique." *Cytological and Clinical Evaluation* **36**, 102–111.

Marcucci M.C., Rodriguez J., Ferreres F., Bankova V., Groto R., Popov S. (1998) "Chemical composition of Brazilian propolis from Sao Paulo state." *Z. Naturforsch.* **53c**, 117–119.

Menniti-Ippolito F, Mazzanti G, Vitalone A, Firenzuoli F, Santuccio C. (2008) "Surveillance of suspected adverse reactions to natural health products: the case of propolis." *Drug Saf.* **31**(5), 419-23. [Abstract](#). Natural health products are promoted to the public as equally or more effective and less toxic than conventional drugs. However, some 'natural' medicines are known to have adverse effects. From April 2002 to August 2007, 18 suspected adverse reactions associated with propolis-containing products were reported to the national surveillance system of natural health products, coordinated by the Italian National Health Institute. Sixteen reports concerned allergic reactions (with dermatological or respiratory symptoms), while two concerned the digestive tract. Some of the reactions were serious: six patients were admitted to hospital or visited an emergency department and in two of these a life-threatening event was reported. In seven patients (four of whom were children), an allergic predisposition was indicated. Propolis, a resinous substance collected by honeybees from the buds of living plants, has been used for several purposes (dermatitis, laryngitis, oral ulcers) because of its wide range of suggested activities (antibacterial, antiviral, antifungal, anti-inflammatory, antioxidant and chemopreventive

actions). However, propolis is also a potent sensitizer and should not be used in patients with an allergic predisposition, in particular an allergy to pollen. In Italy, products containing bee derivatives (bee pollen, royal jelly or propolis) are available to the public as food supplements. No label warning of possible adverse reactions is found on the packaging, although it is well known that atopic and asthmatic individuals may be at an increased risk of allergic reactions after using these products. The public and healthcare practitioners should be aware of the risk of allergic reactions to products derived from bees and a warning should be added to the packaging of these products.

Münstedt K, Hellner M, Hackethal A, Winter D, von Georgi R.(2007) "Contact allergy to propolis in beekeepers." *Allergol Immunopathol (Madr)*.**35**(3), 95-100. [Abstract](#). BACKGROUND: Some toothpastes, cosmetics and ointments contain propolis, a bee product, and it is increasingly popular as a dietary supplement. Although propolis is known to cause contact allergy, there have been no studies of the prevalence of this. OBJECTIVES: This study aimed to determine the prevalence of contact allergy to propolis in beekeepers and any relationship between propolis allergy and environmental and physical and mental health characteristics in this group. SUBJECTS AND METHODS: A specially developed instrument which included a validated questionnaire on emotional stability was included in the issues of three German beekeeping journals sent to subscribers in a number of regions (potential readership 35,000). A reference group also completed questionnaire. RESULTS: 1051 questionnaires were returned and 37 cases of allergic reactions to propolis were reported (3.6%). Only 10 of the 37 (27%) beekeepers had recognised the allergy before participating in this study. Propolis contact allergy was significantly associated with lung diseases and other allergic reactions. Only some affected beekeepers protected their hands more while working with bees and showed significantly greater emotional instability than those not sensitised to propolis. CONCLUSIONS: Contact allergy to propolis is common among beekeepers, but they do not seem to recognise the problem or protect themselves properly.

Naito Y, Yasumuro M, Kondou K, Ohara N. (2007) "Antiinflammatory effect of topically applied propolis extract in carrageenan-induced rat hind paw edema." *Phytother Res*. **21**(5), 452-6. [Abstract](#). The antiinflammatory effect of an ointment containing propolis extract (3%-7%) was examined using carrageenan-induced hind paw edema in rats. Treatment with the ointment inhibited the edema moderately, and the inhibition was significant at 5% and 7%. Additionally, the effect of the ointment on chemotaxis of human polymorphonuclear leukocytes (PMNs) was investigated using the agarose plate method. Migration of PMNs toward zymosan-treated serum was inhibited in the presence of 5% propolis ointment. These results demonstrate that topical application of propolis extract is effective in inhibiting carrageenan-induced rat hind paw edema, and its inhibitory effect on the chemotaxis of PMNs may also contribute to the antiinflammatory effect.

Park Y.K. & Ikegaki M. (1998) "Preparation of water and ethanolic extracts of propolis and evaluation of the preparations." *Biosi Biotech Biochem*.**62**:2230–2232.

Pastor M.A., Martin L., Gatica M.E., Angulo J., Vargas-Machuca I. Del Carmen Farina M. & Requena L. (2003) "Nonoccupational allergic contact dermatitis from propolis." *Actas dermo-sifiliogr*. **94**(3), 188-190. [Abstract](#). Propolis is produced by bees from the resinous secretion of some vegetal species. Allergic contact dermatitis from propolis was originally reported as an occupational disease affecting beekeepers but today involves patients who use «natural» products containing propolis with cosmetic or therapeutical purposes. A case of nonoccupational allergic contact dermatitis from propolis affecting a 44-year-old woman is reported. The patient treated a labial herpes simplex with a solution containing propolis. Some hours later she developed an acute dermatitis on the lip and perioral area. Patch test with the commercial propolis solution was very positive (+ + +) at 48 and 96 hours. Patch test with True Test® showed a positive reaction to balsam of Peru among others. This result may be due to cross reaction, since balsam of Peru shares some components with propolis. The increasing use of topical products marketed as natural cosmetics and drugs could induce a higher frequency of sensitization to propolis in Spain.

Popova M., Bankova V., Chimov A. & Silva M.V. (2002) "A scientific note on the high toxicity of propolis that comes from the Brazilian *Myroxylon balsamum* trees." *Apidologie* **33**, 87-88.

Popova M, Bankova V, Butovska D, Petkov V, Nikolova-Damyanova B, Sabatini AG, Marcazzan GL, Bogdanov S. (2004) "Validated methods for the quantification of biologically active constituents of poplar-type propolis." *Phytochem Analysis*.**15**:235–240.

Ratón J.A., Aguirre A. & Díaz-Pérez J.L. (1990). "Contact dermatitis from propolis." *Contact Dermatitis* **22**, 183-184.

Rudzki E. & Grzywa Z.(1983) "Dermatitis from propolis" *Contact Dermatitis*. **9**(1), 40-5 [Abstract](#). 22 patients with dermatitis from propolis were studied. In all the 21 tests with propolis were positive, and in 19 they were also positive to balsam of Peru. The chromatogram of the balsam and propolis show marked similarity and 3 identical peaks could be recognised in both substances. Among the patients sensitive to balsam of Peru and propolis, 12 were tested with some common components; 3 were positive to cinnamyl cinnamate, 2 to vanillin and 1 to benzyl cinnamate. Chromatograms of the 3 propolis samples from the Warsaw region were very similar, but not identical. Some of the patients were tested with 35 essential oils and eugenol. Sensitivity to clove oil was common.

Suárez D, Zayas D, Guisado F. (2005) "Propolis: Patents and technology trends for health application." *J Bus Chem*. **2**:119–125.

Sforcini J.M., Novelliki ELS, Funarii SRC (2002 "Seasonal effect of Brazillian propolis on seric biochemical variables." *J. Venom. Anim. Toxins* **8**(2) Botucatu. [Abstract](#). Propolis has been the subject of recent scientific investigation due to its biological properties, such as antibiotic, antiinflammatory, anesthetic, healing, immunomodulatory, antioxidant, and carcinostatic. The purpose of this study was to analyze the biochemical profile of propolis-treated rats to observe whether propolis might lead to side effects after administration. Evaluation of total protein, glucose, urea, creatinine, triglycerides, cholesterol, and HDL-cholesterol concentrations and determination of aminotransferases (AST and ALT) and lactic dehydrogenase (LDH) in propolis-treated rat serum were performed. The seasonal effect on propolis activity was also analyzed, considering the biochemical variables evaluated. The lack of clinically important changes in seric biochemical variables is probably because propolis showed no biological side effects under these conditions. A possible seasonal effect on the biochemical determinations was not observed.

Sforcin J.M. (2007) "Propolis and the immune system: a review." *J Ethnopharmacol*. **113**(1), 1-14. [Abstract](#). Propolis has been used empirically for centuries and it was always mentioned as an immunomodulatory agent. In recent years, in vitro and in vivo assays provided new information concerning its mechanisms of action, thus a review dealing with propolis and the immune system became imperative. This review compiles data from our laboratory as well as from other researchers, focusing on its chemical composition and botanical sources, the seasonal effect on its composition and biological properties, its immunomodulatory and antitumor properties, considering its effects on antibody production and on different cells of the immune system, involving the innate and adaptive immune response. In vitro and in vivo assays demonstrated the modulatory action of propolis on murine peritoneal macrophages, increasing their microbicidal activity. Its stimulant action on the lytic activity of natural killer cells against tumor cells, and on antibody production was demonstrated. Propolis inhibitory effects on lymphoproliferation may be associated to its anti-inflammatory property. In immunological assays, the best results were observed when propolis was administered over a short-term to animals. Propolis antitumor property and its anticarcinogenic and antimutagenic potential are discussed. Since humans have used propolis for different purposes and propolis-containing products have been marketed, the knowledge of its properties with scientific basis is not only of academic interest but also of those who use propolis as well. This review opens a new perspective on the investigation of propolis biological properties, mainly with respect to the immune system.

Silvani S., Spettoli E., Stacul F. & Tosti A. (1997). "Contact dermatitis in psoriasis due to propolis." *Contact Dermatitis* **37**, 48-49.

Wanscher B. (1976) "Contact dermatitis from propolis " *British Journal of Dermatology* **94**(4), 451. [Abstract](#). SUMMARY Two patients with contact dermatitis due to the natural product propolis (bee glue) are reported. They presented perioral eczema and stomatitis which were recalcitrant until propolis was considered as the cause. Patch tests with propolis preparations were positive in both patients, and, furthermore, in the second patient the lesions relapsed after provocation tests. European standard patch tests including balsam of Peru were negative. The complexity of propolis, its supposed anti-inflammatory effect due to flavonoids, and the sensitizing agents originating mainly from the poplar trees are discussed together with the cross-sensitization to balsam of Peru. Contact dermatitis due to propolis should be considered in unexplained eczemas, mainly perioral but also in other areas, as propolis preparations are available also as ointments and cosmetic creams.

Wollenweber E., Hausen B.M. & Greenaway W. (1990) "Phenolic constituents and sensitizing properties of propolis, poplar balsam and balsam of Peru." *Bull. Group Polyphen.* **15**, 112–120.