Table II. Within-assay scatter for DHE radioimmunoassay standard curve produced in plasma from rhesus monkey

pmol DHE mesylate ± SD
0.125 ± 0.024
0.25 ± 0.069
0.50 ± 0.082
1.0 ± 0.066
2.0 ± 0.127

tracer were then measured by β-counting after the addition of a scintillator, e.g. Instagel®, Scintisol® complete. Detection was limited to 0.125 pmol DHE per sample (0.5 ml of plasma or serum), corresponding to a ratio (B_x/B_0) of 0.94. The S-shaped standard curve obtained (Figure 1a) was linearized and the best fit was found with the aid of the logit function (Figure 1b).

The antiserum to DHE was also tested for possible cross-reaction with metabolites of DHE. The metabolism of DHE is complex, but it is known that the molecule undergoes cleavage into 2 moieties (Figure 2) thus giving rise to two series of metabolites, derivatives of 9,10-dihydrolysergic acid and derivatives of the peptide moiety (J. R. KIECHEL, unpublished). 50 pmol of 9,10-dihydrolysergic acid failed to give a cross-reaction. With 6 pmol peptide moiety as homologous cyclolcarbonic acid[5], the ratio B_x/B_0 is 0.8, i.e. at this concentration 20% of the cyclolcarbonic acid is bound to antibody.

A practical investigation was then carried out with Dihydergot® in rhesus monkeys. The aim of the investigation was to estimate the unchanged drug in the blood after an oral dose of 2 tablets, each containing 2.5 mg DHE mesylate. The blood levels measured after various intervals of time are indicated in Table I in pmol/ml plasma. The within-assay scatter (± SD) at the 95% confidence level (each value based on 4 observations) is given in Table II.

The radioimmunoassay described is a sensitive and specific test for the detection of 9,10-dihydroergotamine in plasma or serum. The steric specificity of the antibody is such that metabolites derived from the two moieties of the molecule (Figure 2) do not cross-react within the range investigated. It has thus proved possible to determine intact ergot alkaloid in pmol quantities, thus permitting direct determination of pharmacokinetic parameters, such as half-life of elimination, with reference to unchanged drug.

[5] A. HOFMANN, *Die Mutterkornalkaloide* (F. Enke Verlag, Stuttgart 1964), p. 88.

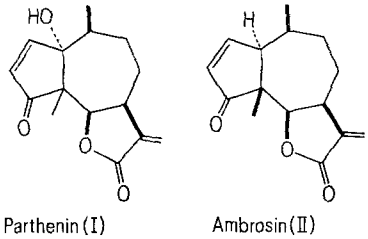
Dermatologically Active Sesquiterpene Lactones in Trichomes of *Parthenium hysterophorus* L. (Compositae)

E. RODRÍGUEZ, M. O. DILLON, T. J. MABRY[1], J. C. MITCHELL[2] and G. H. N. TOWERS[3]

Department of Botany, University of Texas, Austin (Texas 78712, USA), Dermatology Research, Shaughnessy Hospital, Vancouver (B. C., Canada), and Department of Botany, University of British Columbia, Vancouver (B. C., Canada), 30 June 1975.

Summary. Scanning electron microscopy of the leaf surface, phyllaries and achene-complex of *Parthenium hysterophorus* L. showed the presence of 4 types of glandular and non-glandular trichomes. Chemical analysis established the presence of sesquiterpene lactones in the trichomes that cause eczematous dermatitis.

It has been shown recently that a common cause of allergic contact dermatitis in man is the sesquiterpene lactones found commonly in members of the Compositae[4]. The cosmopolitan weed, *Parthenium hysterophorus* L. is currently the cause of a serious outbreak of allergic eczematous dermatitis in parts of India, e.g., Poona, where it was introduced in 1956 from the Americas[5]. The allergenic compounds in this aggressive weed are the pseudoguaianolides, parthenin (I) and ambrosin (II), which are also found in other genera of the Compositae such as *Iva*, *Ambrosia* and *Hymenoclea*[6–10] (Figure 1).



Parthenin (I) Ambrosin (II)

Fig. 1. Allergenic Sesquiterpene Lactones.

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[2] Dermatology Research, Shaughnessy Hospital, Vancouver (B. C., Canada).

[3] Department of Botany, University of British Columbia, Vancouver (B. C., Canada).

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[9] W. HERZ, in *Chemistry in Botanical Classification*. Nobel Symposia 25 (Eds. G. BENDZ and J. SANTESSON; Academic Press, New York 1973).

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External washing of individual plant parts of *P. hysterophorus* with chloroform and subsequent spectral analysis established that the highest concentration of parthenin and ambrosin was in the capitulum and leaves. The capitulum contains up to 8% of its dry weight as sesquiterpene lactones, parthenin being the major component; the abaxial and adaxial leaf surfaces contained 5% sesquiterpene lactones. The stems and roots were devoid of any significant amount of sesquiterpene lactones. Examination by thin-layer chromatography (TLC) of the external washing of the achenes, which are partially covered with capitate-stalked trichomes, also indicated the presence of parthenin and ambrosin. The mature 'achene-complex', which consists of a ray achene and pale, 2 disk-florets and pale, also had a high concentration of sesquiterpene lactones.

Four distinct types of trichomes were detected on the upper and lower leaf surfaces, phyllaries and achenes by SEM. The leaf surface had 2 types: abundant capitate-sessile glands (similar to those observed on the mature bracts of *Cannabis sativa*[11] and *Compositae taxa*[12,13] and uniseriate trichomes (Figures 2 and 3). The phyllaries had 2 types of trichomes, capitate-sessile glandular trichomes and oblong, uniseriate hairs, which were partially covered with protuberances (Figure 4). The disk-floret and pale formed both capitate-sessile glands and multicellular, capitate-stalked glands, which were covered with protuberances (Figure 5). The achene was partially covered with capitate-stalked trichomes.

Examination of the trichome exudates from the leaf of *P. hysterophorus* established that parthenin and ambrosin were present in the trichomes and capitate-sessile glands. Capitate-sessile glands similar to those observed in *P. hysterophorus* are also in species of *Ambrosia*, *Iva*, *Hymenoclea* and *Helenium*, all which produce sesquiterpene lactones. In the genus *Vernonia*, Faust and Jones[14], described in many species which produce sesquiterpene lactones, the presence of bilobed-sessile glands. *Vernonia*

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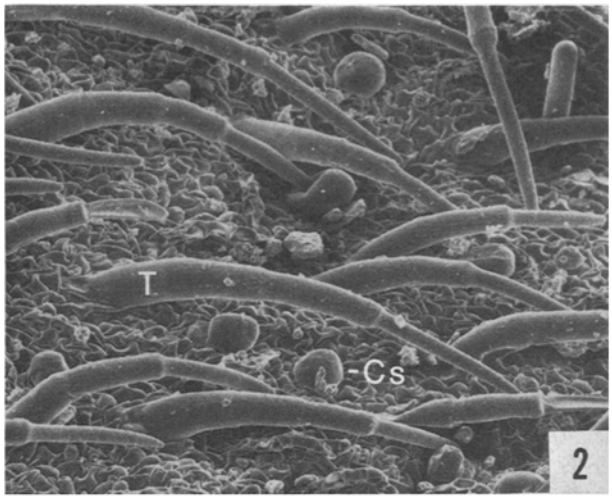

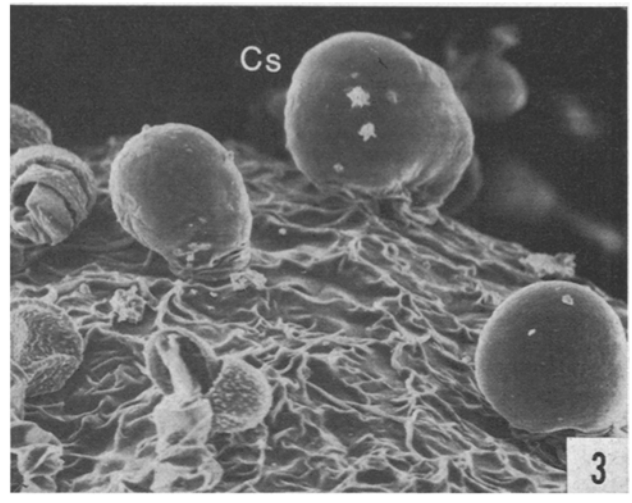

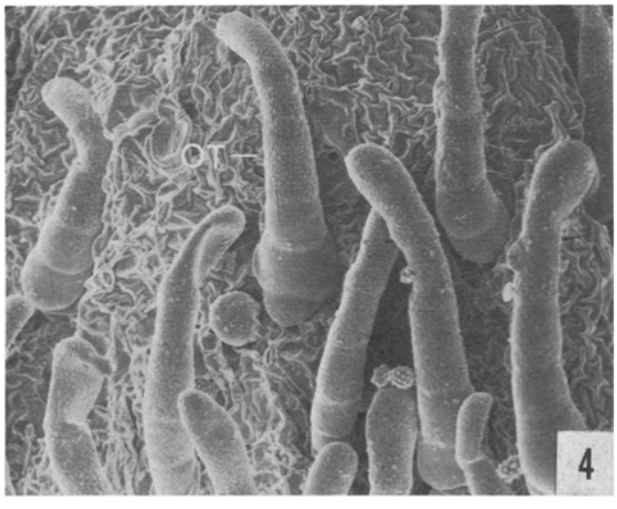

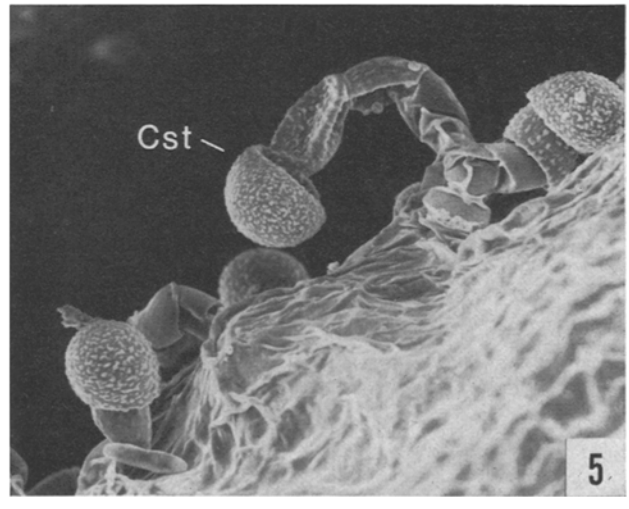

Fig. 2–5. Glandular and non-glandular trichomes on leaf, phyllary, and palea of *Parthenium hysterophorus*. 2. Portion of mature leaf with numerous capitate-sessile glands and multicellular, glandular trichomes. × 200. 3. Bulbous, capitate-sessile gland on disc-floret pale. × 500. 4. Portion of phyllary with oblong, non-glandular trichomes. × 297. 5. Capitate-stalked, non-glandular trichome, present on ray-floret pale and achene. × 500. All specimens were air-dried and coated with gold-paladium (40:60). Cs, capitate-sessile; T. multicellular trichome; OT, oblong, non-glandular trichome; Cst, capitate-stalked trichome.

flaccidifolia was the only species which did not have such glands and PADOLINA[15] later showed that this species did not elaborate sesquiterpene lactones.

Trichomes and their secretory products are recognized as defensive mechanisms against herbivores[16], and since at least one sesquiterpene lactone is known to be an insect feeding deterrent[17], parthenin and ambrosin in the trichomes of *P. hysterophorus* may also function as feeding deterrents.

Allergic contact dermatitis in man results from rupture of the glands and deposition of parthenin and ambrosin on the exposed skin. In India many of the cases of dermatitis from *P. hysterophorus* involve people who do not come in direct contact with the plant (LONKAR, personal communication). The abundance of trichomes on wind-disseminated dried plant parts suggests a mechanism by which city dwellers may develop contact dermatitis from *P. hysterophorus*.

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The Effect of Lithium Carbonate on the Granulocyte Phagocytic Index[1]

A. H. ROSSOF and C. A. COLTMAN, JR.[2]

Hematology-Oncology Service, Department of Medicine and Aerospace Medical Laboratory (Clinical), Wilford Hall USAF Medical Center, CMR No. 8, Box 8344, Lackland AFB (Texas 78236, USA), 31 July 1975.

Summary. Preincubation in lithium carbonate of granulocytes from normal human male volunteer subjects did not alter the ability of these cells to perform properly the ingestion phase of phagocytosis in vitro.

Lithium carbonate (LC) has emerged as effective therapy for patients with manic depressive psychosis[3]. With regularity, patients given this drug develop leukocytosis, characterized by absolute granulocytosis[4–7]. The purpose of this study was to determine the phagocytic indices (PI) of polymorphonuclear neutrophils (PMNs) incubated in vitro for varying periods of time with concentrations of LC covering the therapeutic range and extending into toxic levels (0–5.0 meq/l).

Materials and methods. The technique of PI determination was a modification of the procedure as described by BERG and BRANDT[8].

Heparinized blood was collected by venipuncture in plastic syringes from 4 healthy male volunteer subjects on 6 occasions. The whole blood was spun at $800 \times g$ for 15 min in plastic centrifuge tubes. The buffy coat was removed by suction. Total white blood cell count and differential were determined by hand on an aliquot. The buffy coat was then diluted to 10^4 PMNs/μl with the donor's own plasma. 0.25 ml of the white blood cell suspension was added to LC in phosphate-buffered saline (PBS) to yield a final volume of 0.5 ml with LC concentrations of 0, 0.5, 1.0, 2.0 and 5.0 meq/l. These specimens were prepared in triplicate and incubated for 1, 2 and 4 h at 37 °C in a water bath.

Upon completion of this incubation, 0.5 ml of heat-killed *Torulopsis glabrata* at a concentration of 4×10^4/μl was added to the PMN suspension. This dilution provided an 8:1 ratio of organisms to PMNs. This mixture was incubated at 37 °C for an additional 30 min. The specimens were then spun for 3 min in a small clinical centrifuge. The supernatant was removed and the button was spread and air-dried on a clean glass microscope slide, which was then stained with Wright's stain. 100 granulocytes were counted under oil immersion and scored according to the

[1] The voluntary fully informed consent of the subjects used in this research was obtained as required by AFR No. 169–8.

[2] Acknowledgements. Mr. A. J. RAHE of the Biometrics Division, USAF School of Aerospace Medicine, Brooks Air Force Base, TX. provided the statistical analysis. The LC used in this study was provided through the courtesy of Pfizer, Inc., Brooklyn, N.Y., USA.

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Mean PIs ± 1 SD of PMNs after incubation with varying concentrations of LC (0–5.0 meq/l) for intervals of 1, 2 and 4 hours

Lithium carbonate (meq/l)	Incubation period 1 h	2 h	4 h	Overall mean
0	4.13 ± 1.77	4.04 ± 1.53	4.45 ± 1.49	4.21
0.5	4.32 ± 1.69	4.11 ± 1.58	4.34 ± 1.50	4.26
1.0	3.94 ± 1.56	4.22 ± 1.42	4.15 ± 1.70	4.10
2.0	4.10 ± 1.39	4.14 ± 1.41	4.14 ± 1.52	4.13
5.0	4.31 ± 1.81	4.36 ± 1.58	4.16 ± 1.13	4.28
Overal mean	4.16	4.17	4.25	

Each value represents 6 experiments performed on PMNs from 4 normal healthy male volunteers. The SD are reported for descriptive purposes only and were not used in the statistical testing.