Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Review

The traditional uses, chemical constituents and biological activities of *Plantago major* L. A review

Anne Berit Samuelsen *

*Department of Pharmacognosy, School of Pharmacy, University of Oslo, P.O. Box 1068, Blindern, N-0316 Oslo, Norway

Received 19 March 1999; received in revised form 13 March 2000; accepted 17 March 2000

Abstract

*Plantago major* L. leaves have been used as a wound healing remedy for centuries in almost all parts of the world and in the treatment of a number of diseases apart from wound healing. These include diseases related to the skin, respiratory organs, digestive organs, reproduction, the circulation, against cancer, for pain relief and against infections. *P. major* contains biologically active compounds such as polysaccharides, lipids, caffeic acid derivatives, flavonoids, iridoid glycosides and terpenoids. Alkaloids and some organic acids have also been detected. A range of biological activities has been found from plant extracts including wound healing activity, anti-inflammatory, analgesic, antioxidant, weak antibiotic, immuno modulating and antiulcerogenic activity. Some of these effects may attribute to the use of this plant in folk medicine. © 2000 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Traditional uses; Chemical constituents; Biological activities; *Plantago major* L

1. Botany

*Plantago major* L. (*Plantago major* ssp. *major* L.) is a perennial plant that belongs to the Plantaginaceae family. It can become about 15 cm high, but the size varies a lot depending on the growth habitats. The leaves grow in rosettes, and they are ovate to elliptical with parallel venation (5–9). The leaves are glabrous and have an entire or irregularly dentate margin. The flowers are small, brownish-green on long non-ramified spikes.

*P. major* is pollinated by wind, and large amounts of seeds are produced, up to 20 000 per plant (Fægri, 1970; Tutin et al., 1976). The seeds are quite small with an ovate shape (0.4–0.8 × 0.8–1.5 mm) and a slightly bitter taste. The seed endosperm has highly thickened cellulosic walls with the cell lumen filled with oil and protein. It forms the major part of the seeds and surrounds the embryo completely. The seeds are located in capsules (8–16 per capsule) and become sticky in
humid weather due to the swelling of the polysaccharides present in the seed coat (Qadry, 1963). In this manner the seeds can become attached to animals and humans and thereby be spread.

2. History

Research on pollen has shown that *P. major* was introduced to the Nordic countries parallel to the introduction to the first primitive cultivated fields in the stone age nearly 4000 years ago (Jonsson, 1983). *P. major* was spread by man from Europe throughout the world. The Indians named it ‘White man’s footprint’ because it was found everywhere the Europeans had been. This has been adapted into the genus name *Plantago* that is from Latin *planta*, meaning sole of the foot.

*P. major* is a plant that many people know only as a weed, but *P. major* is also an old medicinal plant that has been known for centuries. In Scandinavia this plant is mostly known for its wound healing properties. The common Norwegian and Swedish name for *P. major* is *groblad* meaning ‘healing leaves’.

The traditional use of *P. major* in wound healing is quite old. It was described by the Greek physician Dioscorides in *De materia medica* in the first century. The leaves were prescribed for treatment of dog bites (Roca-Garcia, 1972). From the ‘Vølsuga saga’ it is known that the Vikings used *P. major* leaves for wound healing (Nielsen, 1969). *P. major* was also described in the 12–13th century by the Islamic author Ibn El Beithar having adopted the knowledge from Greek medicine (Fleurentin et al., 1983). Henrik Harpestreng († 1244) from Denmark wrote in ‘Liber Harbarum’ that *P. major* could heal everything that was torn apart. Mixed with honey it was recommended on wounds. Boiled with butter and eaten, it could heal any organ in the human body (Nielsen, 1969).

It was also commonly used in the time of Shakespeare and is mentioned in his play ‘Romeo and Juliet’, Act I, Scene II from the period 1592–1609:

Romeo: Your plantain leaf is excellent for that.
Benvoleo: For what, I pray thee?
Romeo: For your broken shin.

*P. major* was described in ‘Flora Danica’ by Simon Paulli in 1648 as a very efficient wound healing remedy. At that time it was so common in use that even small children knew about it. The nerves were pulled out of the leaves, and then the leaves were applied on the wounds morning and evening. For superficial wounds to heal, it was sufficient to apply the juice from the plant (Brondegaard, 1987). The English apothecary Nicholas Culpeper published ‘The Complete Herbal’ in 1649. The use of plants in the treatment of diseases was based on astrology. At that time people lacked other explanations as to why some plants had certain effects and others not. According to this theory *P. major* is under Venus: ‘It cures the head by its antipathy to Mars and the privities by its sympathy to Venus. There is not a martial disease that it does not cure’. About the medicinal effects he wrote: ‘It is good to stay spitting of blood and bleedings at the mouth, or the making of foul and bloody water, by reason of any ulcer in the reins or bladder’ (Potterton, 1983).

3. Use in traditional medicine

More recent ethnopharmacological studies show that *P. major* is used in many parts of the world and in the treatment of a number of diseases (Table 1): skin diseases, infectious diseases, problems concerning the digestive organs, respiratory organs, reproduction, the circulation, against tumours, for pain relief and for reducing fever.

4. Chemical constituents and their biological activities

4.1. Carbohydrates

The seeds contain the monosaccharides glucose, fructose, xylose and rhamnose as well as the
Table 1
Some uses of *Plantago major* L. in traditional medicine

| Traditional use       | Part of plant | Country                          | References                                      |
|-----------------------|--------------|----------------------------------|------------------------------------------------|
| **Skin**              |              |                                  |                                                 |
| Abscesses             | 1            | Hawaii, Norway, Turkey           | Nagata (1971), Høeg (1974), Yesilada et al. (1995) |
|                       | 1, w         | Guatemala, Turkey                | Cáceres et al. (1987b), Tabata et al. (1994)   |
| Acne                  | 1, w         | Guatemala                        | Cáceres et al. (1987b)                          |
| Anti-inflammatory      | 1, j         | Madeira                          | Rivera and Obón (1995)                         |
|                       | 1            | Cuba                             | Ruiz et al. (1996)                             |
|                       | p, w         | Chile, Panama, Rodrigues         | Hoeg (1974), Rodriguez et al. (1994), Gupta et al. (1979), Gurib-Fakim et al. (1993) |
|                       | 1, c+p, c    | India                            | Jain (1991), Tiwari et al. (1979)              |
| Bee, wasp and         | 1            | India, Iran                       | Joshi et al. (1982), Zagari (1992)            |
| nettle stings         |              |                                  |                                                 |
|                       | 1, j         | Denmark, Norway                  | Brøndegaard (1987), Hoeg (1974)                |
|                       | 1            | USA                              | Hussey (1974)                                  |
|                       | 1, c         | Iran                             | Zagari (1992)                                  |
|                       |              | Guatemala                        | Cáceres et al. (1987b)                          |
| Burns                 | p, c         | India                            | Saklani and Jain (1989), Rao (1981), Jain (1991) |
|                       | 1            | Guatemala, Iran, Norway          | Cáceres et al. (1987b), Zagari (1992), Hoeg (1974) |
|                       | 1, j         | Cook Isl., Denmark, Rarotonga    | Holdsworth (1991), Brøndegaard (1987)          |
|                       |              |                                  |                                                 |
| Cutaneous             | 1, w + l, c  | Brazil                           | Franca et al. (1996)                           |
| leishmaniasis         |              |                                  |                                                 |
| Cuts                  | 1            | India                            | Saklani and Jain (1989)                        |
|                       | 1, c         | Thailand                         | Anderson (1986a)                               |
|                       | 1+l, c       | Denmark, Norway                  | Brøndegaard (1987), Hoeg (1974)                |
| Dermatitis            | 1, w         | Guatemala                        | Cáceres et al. (1987b)                          |
|                       | 1            | Norway                           | Hoeg (1974)                                    |
| Desinfectant for      | 1+l, c+1, w+1, | Denmark, Norway                  | Brøndegaard (1987), Hoeg (1974)                |
| wounds                | j            |                                  |                                                 |
|                       | 1, c+1, w    | Madeira                          | Rivera and Obón (1995)                         |
|                       | 1, mix+a     | Italy                            | Leporatti and Pavesi (1990)                     |
|                       | 1, c         | Cuba                             | Ruiz et al. (1996)                             |
|                       | 1, w         | Thailand                         | Anderson (1986b)                               |
|                       |              | Chile                            | Houghton and Manby (1985)                       |
| Emollient             | 1, w+s, w    | Europe                           | Roca-Garcia (1972)                             |
|                       | 1, j         | Madeira                          | Rivera and Obón (1995)                         |
|                       | 1, w+r       | Iran                             | Zagari (1992)                                  |
| Exanthema             | 1            | Denmark, Guatemala               | Brøndegaard (1987), Cáceres et al. (1987b)     |
| Haemostatic on         | 1, c         | India                            | Rao and Jamir (1982), Jain (1991)              |
| wounds                |              |                                  |                                                 |
| On poison ivy         | 1, h+l, c    | Denmark, Norway                  | Brøndegaard (1987), Hoeg (1974)                |
| dermatitis            |              | USA                              | Duckett (1980)                                 |
| Pruritus              | 1, c         | Iran                             | Zagari (1992)                                  |
| Pusformation in        | 1            | India                            | Joshi et al. (1982)                            |
| impetigo              |              |                                  |                                                 |
| Rosen                 | 1            | Guatemala                        | Cáceres et al. (1987b)                          |
Table 1 (Continued)

| Traditional use          | Part of plant | Country          | References                                      |
|--------------------------|---------------|------------------|------------------------------------------------|
| Soothing effect          | l, w          | Iran, Philippines| Zagari (1992), Lim-Sylianco and Shier (1985)    |
|                          | r             | Iran             | Zagari (1992)                                  |
|                          | l             | Europe           | Zagari (1992), Roca-Garcia (1972), Höeg (1974) |
| Wound healing            | l, w          | Canary Islands, Chile, Darias et al. (1986), Houghton and Manby (1985), Tabata et al. (1994) |
|                          | p             | USA              | Houghton and Manby (1985)                       |
|                          | l, c          | Brazil, Iran     | Guillén et al. (1997), Zagari (1992)           |
|                          | l             | Guatemala, Russia| Cáceres et al. (1987b), Mironov et al. (1983)  |
|                          | l, c+l, w+l, j| Denmark, Norway  | Brondegaard (1987), Höeg (1974)                |
|                          | l, j          | Cook Islands, Rarotonga |

**Respiratory organs**

| Traditional use          | Part of plant | Country          | References                                      |
|--------------------------|---------------|------------------|------------------------------------------------|
| Anti tussive             | l, w, mix     | Iran             | Zagari (1992)                                  |
|                          | l, j+honey    | Iran             | Zagari (1992)                                  |
| Asthma, bronchitis       | l, r, w       | Iran, Bulgaria   | Zagari (1992), Markov (1992)                   |
| Colds                    | p, w          | Panama           | Gupta et al. (1979)                            |
|                          | l, w          | Norway           | Höeg (1974)                                    |
| Ear ache                 | l, r, w       | Iran             | Zagari (1992)                                  |
| Expectoract              | l, w          | Brazil           | Guillén et al. (1997)                          |
| Pulmonary diseases       | l             | Hawaii           | Nagata (1971)                                  |
|                          | l, w          | Norway, Peru     | Höeg (1974), Ramirez et al. (1988)             |
|                          | s, w          | Europe           | Roca-Garcia (1972)                             |
| Throat inflammation      | f, mix, w     | Iran             | Zagari (1992)                                  |

**Digestive organs**

| Traditional use          | Part of plant | Country          | References                                      |
|--------------------------|---------------|------------------|------------------------------------------------|
| Cholera                  | l, w          | Haiti            | Weniger et al. (1986)                           |
| Constipation             | r, w          | California, USA  | Bocek (1984)                                   |
|                          | s             | India            | Jain (1991)                                    |
| Diarrhea                 | tng           | Mexico           | Ponce-Macotela et al. (1994)                    |
|                          | l, w          | Canary Islands   | Darias et al. (1986)                           |
|                          | j+l, w        | India            | Joshi et al. (1982), Jain and Puri (1984), Jain (1991) |
|                          | l, r, w       | Iran             | Zagari (1992)                                  |
| Dysenteri                | j             | USA              | Eli Lilly (1898)                               |
|                          | s, w          | India            | Joshi et al. (1982)                            |
| Gastritis and colitis    | j, a          | Russia           | Mironov et al. (1983)                          |
| Gum inflammation        | l, w          | Philippines      | Lim-Sylianco and Shier (1985)                   |
| Oral wounds              | l, w          | Brazil           | Guillén et al. (1997)                          |
| Stomach ache             | p, w          | Argentina, USA   | Spring (1989), Bustos et al. (1996)            |
| Stomach cramps           | l, w          | Guatemala        | Logan (1973)                                   |
| Stomatitis               | l, r, w       | Iran             | Zagari (1992)                                  |
|                          | l             | Guatemala        | Cáceres et al. (1987b)                         |
| Ulcer                    | l, w          | Brazil, Norway, Turkey | Höeg (1974), Yesilda et al. (1993), Guillén et al. (1997) |
|                          | p, w          | Argentina, Panama| Gupta et al. (1979), Bustos et al. (1996)      |
|                          | l, w+j        | Russia           | Mironov et al. (1983)                          |
|                          | s, w          | India            | Joshi et al. (1982)                            |

**Urogenital system**

| Traditional use          | Part of plant | Country          | References                                      |
|--------------------------|---------------|------------------|------------------------------------------------|
| Abortifacient            | r             | New Mexico, USA  | Conway and Slocumb (1979)                       |
|                          | s             | India            | Saki and Jain (1989)                           |
| Contraceptive            | l, w          | Afghanistan      | Hunte et al. (1975)                            |
|                          | p, w          | USA (Hmong refugees) | Spring (1989)                             |
| Traditional use                     | Part of plant | Country                  | References                                      |
|-----------------------------------|---------------|--------------------------|------------------------------------------------|
| Inhibit menstrual                  | l, w          | Afghanistan              | Hunte et al. (1975)                              |
| period                             |               |                          |                                                 |
| Kidney stones                      | l, w          | Greece                   | Lawrendiadis (1961)                              |
|                                  | l, w, mix     | Venezuela                | Morton (1975)                                   |
| Menstrual disorders               | j             | USA                      | Eli Lilly (1898)                                 |
|                                  | s             | India                    | Fazal (1979)                                    |
|                                  | r             | South Africa             | Veale et al. (1992)                              |
| Pregnancy and childbirth          | l, j          | Panama                   | Gupta et al. (1979)                              |
| Renal bladder ailments            | p, w          | USA (Hmong refugees)     | Spring (1989)                                   |
| Urinary tract infections          | l, r, w       | Iran                     | Zagari (1992)                                   |
|                                   | l             | Guatemala                | Cáceres et al. (1987b)                           |
|                                   | s, w          | India                    | Joshi et al. (1982)                              |
| Uterine problems                  | p, w          | Rodrigues                | Gurib-Fakim et al. (1993)                        |
| Vaginitis                          | l             | Guatemala                | Cáceres et al. (1987b)                           |
| Heart and circulation             |               |                          |                                                 |
| Astringent effect                 | l, w + r, mix | Iran                     | Zagari (1992)                                   |
|                                  | l, r, w       | India                    | Kapur (1983)                                    |
| Blood rectifier                   | l, w + r      | Iran                     | Zagari (1992)                                   |
| Diabetes                          | l, w + p, w   | Chile                    | Houghton and Manby (1985), Rodriguez et al. (1994) |
| Diuretic                          | s, w          | Vietnam                  | Doan et al. (1992)                               |
|                                  | ng            | New Mexico, USA          | Conway and Slocumb (1979)                        |
|                                  | p, w          | Chile, Rodrigues,        | Rodriguez et al. (1994), Gurib-Fakim et al. (1993), Wasuwat (1967) |
|                                   |               | Thailand                 |                                                 |
|                                   | l, w          | Guatemala                | Cáceres et al. (1987a)                           |
|                                   | w, mix        | China                    | Pan and Lay (1966)                               |
|                                   | j             | USA                      | Eli Lilly (1898)                                 |
|                                   | l, w          | India                    | Joshi et al. (1982)                              |
| Edema                             | l             | Turkey                   | Yesilada et al. (1995)                           |
|                                   |               |                          |                                                 |
| Hemorrhoids                       | l, w          | Brazil, India            | Guillén et al. (1997), Joshi et al. (1982)       |
|                                  | r, w          | Denmark                  | Brøndegaard (1987)                               |
| Hypertension                      | w             | Burma                    | Kyi et al. (1971)                                |
|                                   | l, w          | Hawaië                   | Nagata (1971)                                   |
| Sense organs                      |               |                          |                                                 |
| Eye infections                    | p, w          | Rodrigues                | Gurib-Fakim et al. (1993)                        |
|                                  | l             | Guatemala                | Cáceres et al. (1987b)                           |
|                                  | w             | Panama                   | Gupta et al. (1979)                              |
| Eye problems                      | l, j          | Haiti, Madeira           | Weniger et al. (1986), Rivera and Obón (1995)    |
|                                  | l             | Norway                   | Heeg (1974)                                      |
|                                  | l, w          | Peru, Tobago             | Ramirez et al. (1988), Seaforth et al. (1998)    |
| Nerve system                      |               |                          |                                                 |
| Analgesic                         | l, w          | Brazil, Peru             | Guillén et al. (1997), Ramirez et al. (1988)     |
|                                  | p, w          | USA (Hmong refugees)     | Spring (1989)                                   |
| Antipyretic                        | r, w          | California, USA          | Bocek (1984)                                     |
|                                  | p, w          | Brazil                   | Brandao et al. (1985)                            |
|                                  | l, w          | Brazil, Columbia         | Guillén et al. (1997), Schultes and Raffauf (1994) |
|                                  | l, r, w       | India                    | Joshi et al. (1982), Jain (1991)                 |
Table 1 (Continued)

| Traditional use | Part of plant* | Country | References |
|-----------------|----------------|---------|------------|
| Hypnotic        | l, w, mix      | Venezuela | Morton (1975) |
| Nervous shock   | l, w           | Haiti   | Weniger et al. (1986) |
| Physical weakness | l             | Hawaii  | Nagata (1971) |
| Stimulant       | s, w           | India   | Joshi et al. (1982), Jain (1991) |
|                 | l              | Hawaii  | Nagata (1971) |
|                 | p, w           | Rodrigues | Gurib-Fakim et al. (1993) |
| Toothache       | p, w           | Rodrigues | Gurib-Fakim et al. (1993) |
|                 | l, r, w        | Iran     | Zagari (1992) |
| Antineoplastic  | Tumors         | Canary Islands | Darias et al. (1986) |
|                 | p, w           | Chile, Venezuela | Morton (1975), Bhakuni et al. (1976), Rodriguez et al. (1994) |
|                 | l, j           | Panama  | Gupta et al. (1979) |
| Parasitic infections | Antihelmintic | p         | Argentina, Rodrigues | Gurib-Fakim et al. (1993), Bustos et al. (1996) |
|                 | l, w           | Guatemala | Logan (1973) |
|                 | p              | Tanzania | Weenen et al. (1990) |
| Parasites       | w              | Mexico  | Ponce-Macotela et al. (1994) |
| Skeleton        | For bone fractures | p      | USA (Hmong refugees) | Spring (1989) |
| Antidote        | Snake poison   | p         | USA | Hussey (1974) |
|                 | l, p, c, j     | India    | Jain and Puri (1984), Selvanayagam et al. (1994) |

* f, Flowers; l, leaves; s, seeds, r, root; p, whole plant; c, crushed; j, juice; w, water extract; a, alcohol extract; mix, mixed with other plants; and ng, not given.

disaccharide sucrose and the trisaccharide planteose (\(O-\alpha-D-Gal\p-(1 \rightarrow 6)-O-\beta-D-Fru\p-(2 \rightarrow 1)-\alpha-D-Glc\p\)) (Ahmed et al., 1965). Planteose acts as a reserve carbohydrate in the seeds (Rohrer, 1972).

The outer seed coat contains polysaccharides that swell in contact with water and form mucilage with high viscosity. Polysaccharides extracted from the seeds with cold water are composed of 61% xylose, 13.2% arabinose and 24% galacturonic acid, and the hot water extract of the residue contains 78% xylose, 13.2% arabinose, 3% galactose and 6.2% galacturonic acid (Ahmed et al., 1965). Sa-\m uelsen et al. (1999a) found that the polysaccharides in the 50°C water extract are composed of 39.7% xylose, 13.1% arabinose, 17.2% galacturonic acid, 15.5% glucuronic acid, 2.1% rhamnose, 2.5% galactose and 9.9% glucose. The acidic fractions are heteroxylans that consist of blocks of \(\beta-(1 \rightarrow 4)\)-linked xylose residues and blocks of \(\beta-(1 \rightarrow 3)\)-linked xylose residues in the polymer backbone. Small side chains such as single xylose and arabi-
1.5–3 g/day (Gorin et al., 1966). Given in a dose of 1 mg/kg, plantaglucid reduced the ulceration index in rats stomachs 20 times. In dogs it intensified the secretion of gastric juice. Plantaglucid lowered the tone and reduced the range of contractions in isolated rabbit intestine and also had spasmolytic effect. It helped to reduce inflammatory oedema provoked by formalin and dextran. No toxic effects were observed after prolonged enteral administration to rats and dogs (Obolentseva and Khadzhai, 1966).

A highly esterified pectin polysaccharide with Mw 46–48 kDa, PMII was isolated from a 50°C water extract (Samuelsen et al., 1995, 1996). PMII contains both smooth polygalacturonan and two different ramified regions; one (PVA) that has relatively high amounts of (1→4)- and (1→3,6)-linked galactose residues with arabinose linked to position 6. The side chains in PVA were linked to position 4 of the rhamnose residues in the backbone. The other ramified region (PVb) contained arabinose side chains attached to position 3 of the galacturonic acid residues in the backbone. PMII had high anti-complementary activity, and PVA was the part of PMII that had the highest activity. PMII also activated human monocytes in vitro for increased production of tumour necrosis factor α (TNFα). The pectin fraction that was isolated from the 100°C water extract had very low anti-complementary activity compared to PMII, and this may be due to less of the side chains that were in PVA (Samuelsen et al., 1995, 1996). Lately it was shown that PMII activates complement mainly via the classical pathway (Michaelsen et al., 1999) and that it has prophylactic activity against Staphylococcus pneumoniae infection in mice (Hetland et al., 1999). From the 50°C water extract an anti-complementary acidic arabinogalctan, PMIa, was isolated (Samuelsen et al., 1998). It was composed of arabinose (31%), galactose (32%), rhamnose (6%) and galacturonic acid (7%). This arabinogalctan consists of a (1→3)-linked galactan backbone with (1→6)-linked galactan side chains with arabinose residues attached to position 3 of galactose residues in the side chains. It also contains 1.5% protein with relatively high amounts of hydroxy proline (28.7%), alanine (14.9%) and serine (10.9%) indicating that this is an arabinogalactan type II due to the classification made by Aspinall (1973). The neutral fraction of the water extract had very low anti-complementary activity and consisted of high amounts of glucose and mannose (Samuelsen et al., 1995).

According to a review article on immuno stimulants from higher plants by Wagner (1987) P. major was previously investigated for immunologically active polysaccharides. The isolated polysaccharides increased phagocytosis 15–50% in two in vitro phagocytosis models, and the highest rate of stimulation was achieved with a 0.1 mg/ml aqueous solution. The types of polysaccharides investigated were not stated. The polysaccharides that have been isolated from P. major are summarised in Table 2.

### Table 2
Polysaccharides in *Plantago major* L.

| Polysaccharide               | References                      |
|------------------------------|--------------------------------|
| In leaves                    |                                |
| Plantaglucide                | Pectic acid, galactoarabinan, galactan | Gorin (1966a), Gorin (1966b) |
| PMII                         | Pectin with smooth and hairy regions | Samuelsen et al. (1996) |
| PMIa                         | Arabinogalactan type II         | Samuelsen et al. (1998) |
| Glucomannan                  |                                 | Samuelsen et al. (1995) |
| In seeds                     |                                |
| Starch                       |                                 | Samuelsen et al. (1999a) |
| Acidic heteroxylans          |                                 | Samuelsen et al. (1999a) |

4.2. Lipids

Fatty acids, both free and after hydrolysis of triglycerides, have been isolated from the seeds and are listed in Table 3. According to Ahmed et al. (1968) 64.8% of the fatty acids are unsaturated.

Arachidic acid was isolated from *P. major* seeds only and not from any other *Plantago* species investigated. Most of the fatty acids present are generally found in plant seeds. One unusual hydroxyolefinic fatty acid, 9-hydroxy-cis-11-octadecenoic acid which is an isomer of ricinoleic acid was...
isolated by Ahmad et al. (1980). It is a minor constituent (1.5%) of the seed oil.

From the fresh leaves 0.18% lipids were isolated, and the distributions of the different fatty acids are listed in Table 4. The unsaturated fatty acids, 18:3ω3 and 18:2ω6 and the saturated fatty acid palmitic acid were most abundant in the leaves.

The major components of the leaf wax are the free triterpene acids, oleanolic and ursolic acid (see Other terpenoids), and the linear alkanes C27H56- C33H58. The chloroform extract was composed of about 63% triterpenic acids, 17% linear hydrocarbons, 1% linear alcohols and 19% unidentified compounds independently of the plants age (Bakker et al., 1998).

Clinical and histological studies made by Mironov et al. (1983) showed that saturated C26–C30 primary alcohols with even numbers of carbon atoms from the n-hexane extract and the non-hydrolysable fractions of the n-hexane extract had powerful curative effects on superficial injuries in rabbits.

4.3. Alkaloids

*P. major* has been tested positive for alkaloids (Rojas, 1968; Smolenski et al., 1974). Schneider (1990) identified them as indicain and plantagonin (Fig. 1).

4.4. Caffeic acid derivatives

The ethyl and methyl esters of caffeic acid were isolated from the methanolic extract (Pailer and Haschke-Hofmeister, 1969), and chlorogenic and neochlorogenic acid were isolated from the

---

### Table 3

Fatty acids isolated from the seeds of *Plantago major* L.

| Fatty acid                  | Percent of total fatty acids | References                      |
|----------------------------|------------------------------|---------------------------------|
| Myristic acid              | 14:0                         | Swiatek et al. (1980)           |
| Palmitic acid              | 16:0                         | Ahmed et al. (1968), Swiatek et al. (1980) |
| Stearic acid               | 18:0                         | Ahmed et al. (1968), Swiatek et al. (1980) |
| Oleic acid                 | 18:1 37.4                    | Ahmed et al. (1968), Swiatek et al. (1980) |
| Linoleic acid              | 18:2 25.3                    | Ahmed et al. (1968), Swiatek et al. (1980) |
| Linolenic acid             | 18:3 0.9                     | Ahmed et al. (1968), Swiatek et al. (1980) |
| Arachidic acid             | 20:0                         | Ahmed et al. (1968)             |
| Behenic acid               | 22:0                         | Ahmed et al. (1968)             |
| Lignoceric acid            | 24:0                         | Pailer and Haschke-Hofmeister (1969) |
| 9-Hydroxy-cis-11-octadecenoic acid | 18:1 1.5 | Ahmad et al. (1980) |

---

### Table 4

Fatty acids in *Plantago major* L. leaves (Guil et al., 1996)

| Fatty acid                  | %   |
|-----------------------------|-----|
| Myristic acid               | 14:0 1.8 |
| Palmitic acid               | 16:0 15.9 |
|                             | 16:1ω7 1.5 |
|                             | 16:1ω9 0.1 |
|                             | 16:2ω6 0.4 |
|                             | 16:3ω3 1.0 |
| Stearic acid                | 18:0 2.1 |
|                             | 18:1ω9 2.3 |
|                             | 18:2ω6 11.2 |
|                             | 18:3ω3 33.3 |
|                             | 18:4ω3 2.0 |
| Arachidic acid              | 20:0 1.3 |
|                             | 20:4ω6 1.0 |
|                             | 20:5ω3 1.3 |
| Behenic acid                | 22:0 1.3 |
|                             | 22:1ω9 3.5 |
|                             | 22:6ω3 1.5 |
|                             | 24:0 1.0 |

---

Fig. 1. Alkaloids in *P. major* L. Indicain: R = CHO; plantagonin: R = COOH.
Fig. 2. Caffeic acid derivatives in *P. major* L. (A) Caffeic acid, (B) chlorogenic acid, (C) Plantamajoside R = Glc, acteoside R = Rha.

aqueous extract (Maksyutina, 1971b). According to Noro et al. (1991) plantamajoside is the main caffeic acid derivative in *P. major* L., and only small amounts of acteoside (synonym to verbascoside) are present. Skari et al. (1999a) on the other hand isolated equal amounts of each compound from the 80% ethanol extract of the plant. According to Molgaard (1986), plantamajoside and acteoside are not found together in the same plant. In Denmark, there are two subspecies of *P. major*, *P. major* ssp. major and ssp. spleiosperma. Plantamajoside is present in both subspecies, while acteoside is found only in ssp. spleiosperma (Mølgaard, 1986). Plantamajoside is glycosylated with glucose to the central glucose while in acteoside it is glycosylated with rhamnose (Fig. 2).

Plantamajoside has some known biological activities. It has an inhibitory effect on arachidonic acid-induced mouse ear oedema, i.e. anti-inflammatory activity (Murai et al., 1995), inhibitory activity on 5-lipoxygenase (Ravn et al., 1990), 15-lipoxygenase (Skari et al., 1999a) and cAMP phosphodiesterase (Ravn et al., 1990) and antioxidant activity (Miyase et al., 1991). Skari et al. (1999a) found that plantamajoside is a DPPH (diphenylpicrylhydrazyl) radical scavenger. Plantamajoside is also known to have some antibacterial activity (Ravn and Brimer, 1988).

Aqueous extract (Maksyutina, 1971b). According to Noro et al. (1991) plantamajoside is the main caffeic acid derivative in *P. major* L., and only small amounts of acteoside (synonym to verbascoside) are present. Skari et al. (1999a) on the other hand isolated equal amounts of each compound from the 80% ethanol extract of the plant. According to Molgaard (1986), plantamajoside and acteoside are not found together in the same plant. In Denmark, there are two subspecies of *P. major*, *P. major* ssp. major and ssp. spleiosperma. Plantamajoside is present in both subspecies, while acteoside is found only in ssp. spleiosperma (Mølgaard, 1986). Plantamajoside is glycosylated with glucose to the central glucose while in acteoside it is glycosylated with rhamnose (Fig. 2).

Plantamajoside has some known biological activities. It has an inhibitory effect on arachidonic acid-induced mouse ear oedema, i.e. anti-inflammatory activity (Murai et al., 1995), inhibitory activity on 5-lipoxygenase (Ravn et al., 1990), 15-lipoxygenase (Skari et al., 1999a) and cAMP phosphodiesterase (Ravn et al., 1990) and antioxidant activity (Miyase et al., 1991). Skari et al. (1999a) found that plantamajoside is a DPPH (diphenylpicrylhydrazyl) radical scavenger. Plantamajoside is also known to have some antibacterial activity (Ravn and Brimer, 1988).

Acteoside has superoxide anion and DPPH radical scavenging activities, has antioxidant activity and inhibits lipid peroxidation (Xiong et al., 1996; Miyase et al., 1991; Zhou and Zheng, 1991; Skari et al., 1999a,b). It inhibits 15-lipoxygenase slightly less efficient than plantamajoside (IC$_{50}$ 117 vs. 96 μM) (Skari et al., 1999a). Acteoside inhibits protein kinase C by interacting directly with the catalytic domain of the enzyme (Herbert et al., 1991). Acteoside inhibits aldose reductase (Ravn et al., 1990) and 5-HETE formation (Kimura et al., 1987). It has antibacterial (Shoyama et al., 1987), immunosuppressant (Sasaki et al., 1989) and analgesic activity (Andary et al., 1982). Acteoside has antihypertensive effect, at a dose of 10 mg/kg on rats a significant decrease in systolic, diastolic and mean arterial blood pressure was observed (Ahmad et al., 1995). The biological activities of these and other caffeic acid derivatives are reviewed in Jiménez and Riguer (1994).

4.5. Flavonoids

Several flavonoids have been isolated from *P. major* (Table 5). According to Kawashyty et al. (1994) the amount of each flavonoid isolated from Egyptian *P. major* can be ranged as follows: luteolin 7-glucoside > hispidulin 7-glucuronide > luteolin 7-diglucoside > apigenin 7-glucoside ≈ nepetin 7-glucoside > luteolin 6-hydroxy 4’-methoxy 7-galactoside. Skari et al. (1999b) isolated plantaginin and homoplantaginin in addition to several flavonoids having structures that have not been found in *P. major* earlier. Their structures remain to be published.

Many flavonoids are antioxidants (Rice-Evans et al., 1996; Bohm et al., 1998). Examples of such compounds in *P. major* are baicalein, hispidulin and plantaginin (Yuting et al., 1990; Yokozawa et al., 1997; Skari et al., 1999b). A number of flavonoids are also known to have free radical scavenging activity (Kandaswami and Middleton, 1994). Baicalein, hispidulin, scutallarein and plantaginin are free radical scavengers and inhibit lipid peroxidation (Sanz et al., 1994; Yoshino et al., 1997; Gao et al., 1999; Skari et al., 1999b). Both baicalein and hispidulin have anti-inflammatory activity. Baicalein inhibits carrageenan-induced rat paw edema (Lin and Shieh, 1996a), 12-lipoxygenase (You et al., 1999) and LPS induced production of nitric oxide in macrophages (Wakabayashi, 1999) while hispidulin has been shown to be an inhibitor of 5-lipoxygenase (Moongkarndi et al., 1991). Baicalein has hepatop-
Table 5
Flavonoids in *Plantago major* L. compound

| Compound | 3 | 5 | 6 | 7 | 8 | 2' | 3' | 4' | 5' | 6' | References* |
|----------|---|---|---|---|---|----|----|----|----|----|--------------|
| Apigenin 7-glucosid | H | OH | H | OGl | C | H | H | H | OH | H | H | 3 |
| Baicalein | H | OH | OH | OH | H | H | H | H | H | H | 1 |
| Hispidulin | H | OH | OMe | OH | H | H | H | OH | H | H | 2 |
| Hispidulin 7-glucuronide | H | OH | OMe | OGl | A | H | H | H | OH | H | H | 3 |
| Homoplatagninin | H | OH | OMe | OGl | C | H | H | H | OH | H | H | 4, 5 |
| Luteolin 7-glucosid | H | OH | H | OGl | C | H | H | OH | OH | H | H | 3 |
| Luteolin 7-diglucosid | H | OH | H | OGl-Glc | C | H | H | OH | OH | H | H | 3 |
| Luteolin 6-hydroxy-4-methoxy-7-galactoside | H | OH | OH | OGal | H | H | OH | OH | OH | Me | H | 3 |
| Nepetin 7-glucoside | H | OH | OMe | OGl | C | H | H | OH | OH | OH | H | 3 |
| Plantaginin | H | OH | OH | OGl | C | H | H | H | OH | H | H | 4, 5 |
| Scutellarein | H | OH | OH | OH | H | H | H | OH | OH | H | H | 1, 2 |

* References: 1, Maksyutina (1971a); 2, Harborne and Williams (1971); 3, Kawashty et al. (1994); 4, Nishibe et al. (1995); and 5, Skari et al. (1999b).
protective effect against CCl₄-induced liver injuries in rats (Lin and Shieh, 1996b). Baicalein can induce cell death of carcinoma cells (Matsuzaki et al., 1996), cause inhibition of cell growth of human hepatoma cells (Motoo and Sawabu, 1994) and has shown strong antiproliferative effect in rat hepatic stellate cells (Inoue and Jackson, 1999). Scutellarein and baicalein have antiallergic activities (Kawasaki et al., 1994; Toyoda et al., 1997). In addition, they are HIV-reverse transcriptase inhibitors in vitro; (IC₅₀ 2.5 and 5.6 µM, respectively). The glucosides plantaginin, luteolin 7-glucoside and homoplantaginin are also potent inhibitors (IC₅₀ 9.8, 40.2 and 43.3 µM, respectively) while apigenin 7-glucoside had no inhibitory effect on HIV-reverse transcriptase (Nishibe et al., 1997).

4.6. Iridoid glycosides

The iridoid glycosides isolated from _P. major_ are listed in Table 6, and the structure formulas are given in Fig. 3. The major iridoid glycoside found is aucubin, but its content varies over the seasons. The highest aucubin level registered (1.3% in dried leaves) was in June. _P. major_ contains less aucubin than _P. lanceolata_ (Long et al., 1995). Three unusual iridoid glycosides with 8,9 double bonds, majoroside (Handjieva et al., 1991), 10-hydroxy-majoroside and 10-acetoxymajoroside have been isolated from the aerial parts of the plant (Taskova et al., 1999).

Aucubin has anti-inflammatory properties: when applied topically aucubin has an inhibitory effect on TPA (12-O-tetradecanoylphorbol acetate) induced mouse ear oedema with a maximum effect at a dose of 1 mg/ear. This effect is close to that of indomethacin at 0.5 mg/ear (Recio et al., 1994). Aucubin has also spasmolytic properties on acetylcholine induced contraction on rat uterus and rat vas deferens (Oriz de Urbina et al., 1994). Aucubin has antidote activity for poisonous amanita mushrooms in mice by protection against liver damage induced by z-amanitin. The mechanism is thought to be due to a competitive effect of aucubin on z-amanitin inhibition of liver RNA synthesis (Chang et al., 1984). It also has liver protective activity against CCl₄-induced hepatic damage in mice (Chang, 1998) in addition to antiviral activity against hepatitis B virus (Chang, 1997).

The aglycon of aucubin, aucubigenin, has antimicrobial activity against bacteria and moulds (Davini et al., 1986).

4.7. Other terpenoids

The terpenoid loliolid has been isolated from the leaves (Pailer and Haschke-Hofmeister, 1969).
The triterpenoids oleanolic acid, ursolic acid, 18β-glycyrrhetinic acid and sitosterol were isolated from the leaf wax (Hiltibran et al., 1953; Ringbom et al., 1998). Ursolic acid inhibits cyclooxygenase-2 (IC50 130 μM) and cyclooxygenase-1 (IC50 295 μM) catalysed prostaglandin biosynthesis in vitro while the structural isomer oleanolic acid is less active. 18β-Glycyrrhetinic acid had no significant inhibitory effect (Ringbom et al., 1998). The mechanisms of the anti-inflammatory effects also include inhibition of histamin release from mast cells, inhibition of elastase and inhibition of complement activity. Ursolic acid and oleanolic acid also have hepatoprotective, tumor promotion inhibiting activity and an anti-hyperlipidemic effect (Liu, 1995).

4.8. Glucosinolates

Intact glucosinolates have not been isolated from *P. major* seeds or leaves (Larsen et al., 1983).

4.9. Vitamins

*P. major* has been used as a food supply, especially during spring before the harvest of the common vegetables. The vitamin contents have, therefore, been examined. The fresh leaves of old plants that had gone to seed, collected in early spring, were reported to contain 6 mg β-carotene (provitamin A)/100 g and 19 mg ascorbic acid/100 g (Zennie and Ogzewalla, 1977). According to a study of young plants *P. major* contains 25 mg ascorbic acid, 31 mg dehydroascorbic acid and 8.5 mg carotenoids/100 g young leaves. Thus, *P. major* can be considered as a good source of vitamin C and carotenoids. In addition, the oxalic acid, nitrate and erucic acid were present in low amounts (67 ± 36 mg/100 g, 101 ± 18 mg/100 g and 3.45%, respectively) indicating a low toxicity of the plant (Guil et al., 1997).

Shoots of *P. major* collected in June contained 37 mg/g dried leaf material of phylloquinone (vitamin K₃). A high vitamin K level might be of importance in the resistance of weeds to the herbicide 2,4 dichlorophenoxyacetic acid. The vitamin K level in *P. major* was intermediate compared to other plant species, and it was also moderately resistant towards the herbicide (Jansson, 1974).

4.10. Other organic acids

From the methanol extract the following organic acids were isolated: fumaric acid, syringic acid, vanillic acid, p-hydroxy benzoic acid, ferulic acid, p-coumaric acid, gentisic acid, traces of salicylic acid, benzoic acid and cinnamic acid (Pailer and Haschke-Hofmeister, 1969).

5. Biological activity of extracts

*P. major* is used for different purposes in traditional medicine around the world, therefore, researchers have tested it for different types of biological activities. Most tests have been performed on crude extracts without examining the nature of the active compounds. The results of these studies are listed below and include both positive and negative results.

5.1. Antitussive activity

*P. major* has been used in Turkey in the treatment of ulcers. The powdered dried leaves were taken together with honey daily before breakfast. A water immersion-stress ulcer model was used on rats to test the plant extract’s ability to inhibit ulcers. A test sample was given just before immobilisation in a stress cage. After 7 h immersed in a water-bath the rats were killed and the stomachs were taken out for examination. The combined methanol- and water extract (1.2 g/kg) inhibited ulcer formation by 40% relative to the control group which received only the vehicle. The water extract (1 g/kg) inhibited ulcer formation by 37% and the methanol extract inhibited it by 29%. *P. major* was not among the most active plants tested (Yesilada et al., 1993).

5.2. Anticancer activity

In a screening of anticancer activity of Chilean plants a 50% ethanol extract of leaves, stems and seeds of *P. major* had no activity in vivo against
lymphocytic leukaemia in mice (Bhakuni et al., 1976).

A *P. major* preparation was reported to be effective in a screening system for prophylactic oncology. The effect included antimetastatic activity in models of tumour metastasis in mice. The details in this study were not described (Yaremchenko, 1990). In another study, an aqueous extract was shown to have a prophylactic effect on mammary cancer in mice (Lithander, 1992). The leaves were extracted with phosphate buffer pH 7 containing 0.9% NaCl and injected subcutaneously in mice of the C3H Strong strain. Among mice of this strain more than 90% develop cancer induced by a virus infection. After 60 weeks, 93.3% of the untreated and 18.2% of the treated mice had tumours. The observed effect is thought to be due to stimulation of the immune system rather than a direct effect on the virus. No experimental results support this idea, only some observations made without experimental verification. The *P. major* extract had good effect on human herpes infections but had no effect on the herpes virus in vitro tests. The same observations have been made for bacteria; only weak antibacterial activity of *P. major* extracts in vitro, but they had an effect on infected wounds in vivo. While antibiotics on infected wounds had no effect, topical treatment with *P. major* extract eradicated the infections and healed the wounds.

5.3. Immunomodulatory activity

The leaves extracted in saline for 2 h at 50°C had chemotactic activity on neutrophils using the Boyden migration chamber method, but it did not enhance neutrophil intracellular killing activity by the nitrozoelblue tetrazolium reduction test (Basaran et al., 1997).

5.4. Antinfective testing in vitro

5.4.1. Antibiotic and antifungal activity

*P. major* has been included in screening studies of plants used in folk medicine in fighting bacterial and fungal infections in the skin or in the treatment of gastrointestinal disorders. Discs containing plant extracts were applied to bacteria cultured on agar plates, and the inhibition zones measured after some time. Water extracts, methanol extracts, 50% and 70% ethanol extracts were tested.

The methanol extracts were most active against *Salmonella typhimurium* (Table 7) and had weaker activity against methicillin resistant *S. aureus* and *M. phlei*. The methanol extracts were active (8–10 mm inhibition zone) against the fungi *F. tricuitum* and *M. gypseum*, and an incomplete inhibition of *C. albicans* and *S. cerevisiae* was observed (Table 8). The antifungal activity was weaker than the antymycoticum nystatin (15–20 mm inhibition zone).

The 50% ethanol extracts were active against *S. aureus*, *B. subtilis*, *S. dysenteriae* and *E. coli*. These include both gram negative and gram positive bacteria. The 70% ethanol extracts were most effective against *S. flexneri* and had weaker activity against *S. aureus*, *S. sonnei*, *E. coli*, *Escherichia ‘crim’* and *M. smegmatis*.

The antibiotic activities registered were weaker than the positive controls used. Incubation of gentimicin and a *P. major* methanol extract gave inhibition zones of > 25 mm and 10–15 mm, respectively on *S. typhimurium*.

In conclusion there seems to be some intermediately polar or nonpolar substances of relatively low molecular weight in *P. major* that have antibiotic activity against some gram negative and gram positive bacteria in addition to a weak antymycotic activity.

5.4.2. Antigiardiasic activity

*P. major* is used in Mexico against diarrhoea and/or parasites. A decoction in a saline solution was made of the plant, and this was incubated with trophozoides of *Giardia duodenalis*. The mortality was 76 ± 1.2 which was at the level of the positive control tinidazol (79 ± 1.9) (Ponce-Macotela et al., 1994).

5.4.3. Antimalarial activity

*P. major* has been used in the treatment of malaria in Tanzania. In vitro activity against *Plasmodium falciparum* strain K, which is multi-drug resistant was performed by measurement of
Table 7
Antibiotic activity of *Plantago major* L. water extract, methanol extract (MeOH), 50% and 70% ethanol extract (EtOH) determined by measurement of inhibition zones of discs containing extracts on bacteria cultures on agar plates

| Bacteria                      | H₂O | MeOH | 50% EtOH | 70% EtOH | References² |
|-------------------------------|-----|------|----------|----------|-------------|
| *Staphylococcus aureus*       |     |      |          |          | 1, 2, 3     |
| *S. aureus*, methicillin resistant |    |      |          |          | 5           |
| *S. aureus*, methicillin sensitive  |     |      |          |          | 5           |
| *Streptococcus pyogenes*      |     |      |          |          | 3           |
| *Bacillus subtilis*           | −   | +    | −        |          | 2, 3, 5     |
| *Shigella sonnei*             |     |      |          |          | 2           |
| *S. flexneri*                 | −/+ | +    |          |          | 2, 3, 4     |
| *S. dysenteriae*              |     |      |          |          | 4           |
| *Salmonella typhi*            | −/− | +    |          |          | 3, 4        |
| *S. enteritidis*              |     |      |          |          | 4           |
| *S. typhimurium*              | +   |      |          |          | 5           |
| *Serratia marcescens*         |     |      |          |          | 5           |
| *Enterobacter aerogenes*      |     |      |          |          | 5           |
| *Escherichia coli*            | −   | −    | +        | +        | 1, 2, 3, 4, 5|
| *Escherichia “crim”*          |     |      |          |          | 2           |
| *Klebsiella pneumonia*        |     |      |          |          | 5           |
| *Pseudomonas aeruginosa*      |     |      |          |          | 3, 5        |
| *Proteus vulgaris*            |     |      |          |          | 3           |
| *Mycobacterium phlei*         |     |      |          |          | 5           |
| *M. smegmatis*                |     |      |          |          | 2           |

¹ Effects as defined by the authors: −, inhibition zone < 6–8 mm; +, inhibition zone 6–10 mm; + +, inhibition zone 10–15 mm.
² References: 1, Gaw and Wang (1949); 2, Moskalenko (1986); 3, Cáceres et al. (1987b); 4, Cáceres et al. (1990); and 5, McCutcheon et al. (1992).

the ability of the extracts to inhibit the incorporation of [³H]-hypoxantine into the malaria parasites. The dichloromethane extract of the whole plant had some effect (IC₅₀ 10–49 mg/ml), the petroleum ether extract and the methanol extract had little activity (IC₅₀ 100–499 mg/ml and < 499 mg/ml, respectively). For comparison, the methanol extract of a *Cinchona* species had an IC₅₀ of 0.5 mg/ml (Weenen et al., 1990).

5.4.4. Antiviral activity

No antiviral activity against herpes and polio virus of ethanol extracts of the entire plant was registered in the in vitro study of Suganda et al. (1983). Neither was the methanol extract of the plant active in vitro against bovine coronavirus, bovine herpesvirus type 1, bovine parainfluenza virus type 3, bovine rotavirus, bovine respiratory syncytial virus, vaccinia virus or vesicular stomatitis virus (McCutcheon et al., 1995).

Table 8
Antifungal activity of *Plantago major* L. methanol extract (MeOH), 50% ethanol extract (EtOH) determined by measurement of inhibition zones of discs containing extracts on bacteria cultures on agar plates

| Fungi                      | MeOH | 50% EtOH |
|----------------------------|------|----------|
| *Aspergillus flavus*       | −    |          |
| *A. fumigatus*             | −    |          |
| *Fusarium tricinctum*      | +    |          |
| *Saccharomyces cerevisiae* | +i   |          |
| *Trichoderma viridae*      | −    |          |
| *Microsporum cockerti*     | −    |          |
| *M. gypseum*               | +    |          |
| *Trichophyton mentagrophytes* | +i |          |
| *Candida albicans*         | +    |          |

¹ Effects as defined by the authors: −, inhibition zone < 6–8 mm; +, inhibition zone 6–10 mm; 1, incomplete inhibition.
5.5. Anti-inflammatory and analgesic activity

The aqueous extract (72°C, 30 min) of dried *P. major* leaves given orally has shown anti-inflammatory and analgesic activities related to inhibition of prostaglandin synthesis in mice and rats. Anti-inflammatory activity in rats was demonstrated by the inhibition of paw oedema induced by carrageenan. The extract did not affect oedema produced by dextran, indicating that the mechanism involved inhibition of cyclooxygenase synthesis rather than an antihistamine activity. The extract also inhibited the formation of exudate and leucocyte mobilisation induced by intrapleural injection of carrageenan, the latter being a known activity of non-steroidal anti-inflammatory compounds. Activity against chronic inflammation was measured as the inhibition of exudate in the air pouch after oral treatment with extract.

Peroral treatment of mice with extract inhibited acetic acid induced writhing (i.e. non-steroid anti-inflammatory activity) but had no effect on the tail flick test (i.e. no opioid-like analgesic activity) (Guillén et al., 1997).

5.6. Antioxidant and free radical scavenger activity

Antioxidant capacity by bleaching of the absorbance of pre-formed 2,2'-azinobis (3-ethylbenzthiazolesulphonic acid) radical cation in the presence of infusions made from *P. major* herbal tea bags and *P. major* leaves were determined. The infusion of *P. major* tea contained small amounts of free radical scavengers compared to black tea. The antioxidants had low reactivity, measured as a relatively high *t*<sub>1/2</sub>. The antioxidant capacity of the green leaves was higher than that of the *P. major* tea indicating that processing can lead to significant loss of activity (Campos and Lissi, 1995).

5.7. Diuretic effect

In Guatemala the leaves are used as a diuretic agent. In a screening study of 67 plants a 10% decoction of the dried leaves of *P. major* was tested on rats. The decoction was administered by a nasogastric catheter at a dose of 1 g/kg. It had an intermediate diuretic activity; urinary output increased by 108 ± 44% after 6 h. Hydrochlorothiazide increased urinary output by 286 ± 38 % (Cáceres et al., 1987a).

In Vietnam, the extracts of the seeds of *P. major* taken orally are said to have a diuretic effect. A possible diuretic activity was tested on healthy human volunteers in a placebo controlled double-blind crossover model. No significant diuretic effect through increased urinary output or sodium excretion was registered in this study (Doan et al., 1992).

5.8. Hypotensive effect

In Burma, the infusion of *P. major* is taken orally to produce a fall in blood pressure. Lipophillic compounds were removed from a *P. major* water extract containing high molecular weight compounds and injected at doses of 15, 20 and 25 mg/kg into anaesthetised dogs. The dose–response effect was not very consistent, and there were large individual variations in the response. The study was of a preliminary nature and without any statistics (Kyi et al., 1971).

In another study normotensive rats were given a *P. major* extract intravenously. The extract was lyophilised 70% ethanol extracts dissolved in a physiological solution. Maximum effect was obtained 0.2 min after injection and lasted for 0.5 min. The reduction in arterial blood pressure was not significant (Schmeda-Hirschmann et al., 1992).

5.9. Hypoglycaemic activity

Rodriguez et al. (1994) have tested a 70% ethanol extract for its hypoglycaemic activity in normoglycaemic rats without finding any significant effect. The extract was given orally at a dose of 500 mg/kg. The background for the testing was that the Mapuche Indians in Chile have used the infusion of *P. major* in the treatment of diabetes (Houghton and Manby, 1985).
Table 9
The toxicity of *Plantago major* L. leaf extracts

| Extract            | Test                                                              | Toxic | Comments                                      | Ref.* |
|--------------------|-------------------------------------------------------------------|-------|-----------------------------------------------|-------|
| Decoction          | Ames test, strains TA 1537 and TA 98                              | +     | Direct frameshift mutagens                    | 1     |
| Decoction          | Ames test strains TA 1537 and TA 98                              | –     | Stimulation of colony growth                  | 2     |
| Alcohol extract    | Plate incorporation assay with *Aspergillus nidulans* D-30       | –     | Stimulation of colony growth                  | 3     |
| Alcohol extract    | *Aspergillus nidulans* somatic segregation assay                  | –     |                                                | 3     |
| 70% Ethanol extract| Brine shrimp (*Artemia salina*)                                  | +     | LC$_{50}$ = 7 µg/ml                          | 4     |
| Not stated         | i.p. and oral administration in rats                             | –     | LD$_{50}$ = 1000 mg/kg i.p.,                  | 5     |
| Saline extract     | COMET assay in human lymphocytes                                 | +     | DNA strand brakeage                           | 2     |

* References: 1, Lim-Sylianco and Shier (1985); 2, Basaran et al. (1996); 3, Ruiz et al. (1996); 4, Schmeda-Hirschmann et al. (1992); and 5, Angelov et al. (1980).

6. Toxicity

As shown in Table 9 the genotoxicity of *P. major* extracts on prokaryotes are somewhat contradictory. In the Ames test (*S. typhimurium* microsomal activation assay), water extracts caused reversions of tester strains TA1537 and TA98. This indicates the presence of direct frameshift mutagens (Lim-Sylianco and Shier, 1985). The *P. major* saline extract had, however, no response in the Ames test with strains TA98 and TA100 (Basaran et al., 1996).

An alcohol extract showed no toxicity on the diploid strain *Aspergillus nidulans* D-30, on the contrary, a stimulation of colony growth was observed. The *A. nidulans* strain used in the somatic segregation assay carry four recessive mutations for conodial colour, and coloured sectors are used as an indicator of genotoxic events leading to somatic segregation. No significant differences in frequency of coloured sectors per colony compared to the negative control were observed. Thus, no genotoxic effect was found of the plant extract (Ruiz et al., 1996).

The 70% ethanol extract was found to be toxic to shrimps (Schmeda-Hirschmann et al., 1992) but *P. major* possesses a low toxicity in rats oral and i.p. administration (Angelov et al., 1980).

DNA damage by strand breakage was suggested after examination of human lymphocytes treated with the saline extract. It had an increased activity in the alkaline COMET assay compared to the negative control (Basaran et al., 1996).

7. Concluding remarks

Taking the claimed wound healing activity of *P. major* into consideration, it is not necessarily only one single compound that is responsible for this effect, the effect may as well be due to several compounds that act in a synergistic manner or to compounds which regulate one another.

There are several of the isolated compounds that may aid the healing of wounds. Plantamajoside and acteoside have antibacterial activities. Some flavonoids and the caffeic acid derivatives plantamajoside and acteoside have antioxidative and free radical scavenging activities. Pectic polysaccharides have been reported to be effective against ulcers in rats and for having immunostimulatory activities. Finally, the long chained saturated primary alcohols that are present in the leaf wax aid the healing of superficial wounds. However, the leaves also contain compounds with anti-inflammatory activity, namely plantamajoside, baicalein, hispidulin, aucubin, ursolic acid and oleanolic acid. Since the inflammatory phase in general is necessary in the wound healing process, anti-inflammatory activity may be undesirable. On the other hand, these substances’ activities when acting together with other compounds present in the leaves are not known at present. Thus, the full picture of *P. major* as a wound healing remedy may be rather intricate.
Due to the very long tradition in using *Plantago major* for wound healing and also because of what is known today about its chemical constituents and biological activities, it seems to be worth the effort of exploring this plant further.

References

Ahmad, M.S., Ahmad, M.U., Osman, S.M., 1980. A new hydroxyolefinic acid from *Plantago major* seed oil. Phytochemistry 19, 217–2139.

Ahmad, M., Rizwani, G.H., Aftab, K., Ahmad, U.V., Gilani, A.H., Ahmad, S.P., 1995. Acteoside: a new antihypertensive drug. Phytotherapy Research 9, 525–527.

Ahmed, Z.F., Rizk, A.M., Hammouda, F.M., 1965. Phytochemical studies of egyptian *Plantago* species (Glucides). Journal of Pharmaceutical Sciences 54, 1060–1062.

Ahmed, Z.F., Hammouda, F.M., Rizk, A.M., Wassel, G.M., 1968. Phychochemical studies of egyptian *Plantago* species. Planta Medica 4, 404–410.

Andary, C., Wylde, R., Laffite, C., Privat, G., Winternitz, F., 1982. Structures of verbascoside and orobanchoside, caffeic acid sugar esters from *Orobanche rapum-genistae*. Phytochemistry 21, 1123–1127.

Anderson, E.F., 1986a. Ethnobotany of hill tribes of northern Thailand. I. Medicinal plants of Akha. Economic Botany 40, 38–53.

Anderson, E.F., 1986b. Ethnobotany of hill tribes of northern Thailand. II. Lahu medicinal plants. Economic Botany 40, 442–450.

Angelov, A., Lambev, I., Markov, M., Yakimova, K., Leseva, M., Yakimov, A., 1980. Study of acute and chronic toxicity of dispergue of *Plantago major*. Medical Archives 18, 47–52.

Aspinall, G.O., 1973. Carbohydrate polymers of plant cell walls. In: Loewus, F. (Ed.), Biogenesis of Plant Cell Wall Polysaccharides. Academic Press, New York pp. 95–115.

Bakker, M.I., Baas, W.J., Sum, D.T.H.M., Koloffel, C., 1998. Leaf wax of *Lactuca sativa* and *Plantago major*. Phytochemistry 47, 1489–1493.

Basaran, A.A., Yu, T.-W., Plewa, M.J., Anderson, D., 1996. An investigation of some Turkish herbal medicines in *Salmonella typhimurium* and in the COMET assay in human lymphocytes. Teratogenesis. Carcinogenesis and Mutagenesis 16, 125–138.

Basaran, A.A., Ceritoglu, I., Undeger, U., Basaran, N., 1997. Immunomodulatory activities of some Turkish medicinal plants. Phytotherapy Research 11, 609–611.

Bhakuni, D.S., Bittner, M., Marticorena, C., et al., 1976. Screening of Chilean plants for anticancer activity. Lloydia 39, 225–243.

Bianco, A., Guiso, M., Passacantilli, P., Francesconi, A., 1984. Iridoid and phenylpropanoid glycosides from new sources. Journal of Natural Products 47, 901–902.

Bocock, B.R., 1984. Ethnobotany of Costanoan indians, California, based on collections by John P. Harrington. Economic Botany 38, 241–255.

Bohm, H., Boeing, H., Hempel, J., Raab, B., Kroke, A., 1998. Flavonols, flavones and anthocyanins as native antioxidants of food and their possible role in the prevention of chronic diseases. Zeitschrift fur Ernahrungswissenschaft 37, 147–163.

Brando, M., Botelho, M., Krettli, E., 1985. Antimarial experimental chemotherapy using natural products. Ciencia e Cultura 37, 1152–1163.

Brodnegaard, V.J., 1987. Folk og Flora, Vol. 4. Rosenkilde and Bagger, Kobenhavn, pp. 68-77.

Bustos, D.A, Tapia, A.A., Feresin, G.E., Espinar, L.A., 1996. Ethnopharmacobotanical survey of Bauchazeta district, San Juan Province, Argentina. Fitoterapia 5, 411–415.

Cáceres, A., Giron, L.M., Martinez, A.M., 1987a. Diuretic activity of plants used for the treatment of urinary ailments in Guatemala. Journal of Ethnopharmacology 19, 223–245.

Cáceres, A., Giron, L.M., Alvarado, S.R., Torres, M.F., 1987b. Screening of antimicrobial activity of plants popularly used in Guatemala for the treatment of dermatomycosal diseases. Journal of Ethnopharmacology 20, 223–237.

Cáceres, A., Cano, O., Samayoa, B., Aguilar, L., 1990. Plants used in Guatemala for the treatment of gastrointestinal disorders. A. Screening of 84 plants against enterobacteria. Journal of Ethnopharmacology 30, 55–73.

Campos, A.M., Lissi, E.A., 1995. Evaluation of the antioxidant capacity of herbal teas by a procedure based on the bleaching of ABTS radical cations. Boletin de la Sociedad Chilena de Quimica 40, 375–381.

Chang, I.M., Yen, H.S., Kim, Y.S., Ahn, J.W., 1984. Aucubin: potential antidote for alpha-amanitin poisoning. Clinical Toxicology 22, 77–85.

Chang, I.M., 1997. Antiviral activity of aucubin against hepatitis B virus replication. Phytotherapy Research 11, 189–192.

Chang, I.M., 1998. Liver-protective activities of aucubin derived from traditional oriental medicine. Research Communications in Molecular Pathology and Pharmacology 102, 189–204.

Chatterton, N.J., Harrison, P.A., Thornley, W.R., Bennett, J.H., 1990. Sucrosyloligosaccharides and cool temperature growth in 14 forb species. Plant Physiology and Biochemistry 28, 167–172.

Conway, G.A., Stocumb, J.C., 1979. Plants used as abortifacients and emmenagogues by spanish New Mexicans. Journal of Ethnopharmacology 1, 241–261.

Darias, V., Bravo, L., Barquin, E., Herrera, D.M., Fraile, C., 1986. Contribution to the ethnopharmacological study of the Canary Islands. Journal of Ethnopharmacology 15, 169–193.

Davini, E., Lavarone, C., Trogolo, C., Aureli, P., Pasolini, B., 1986. The quantitative isolation and antimicrobial activity of the aglycone of aucubin. Phytochemistry 25, 2420–2422.
Kawasaki, M., Toyoda, M., Teshima, R., et al., 1994. In vitro anti-<n>allergic</n> activity of flavonoids in histamine-release assay using rat basophilic leukemia (RBL-2H3) cells. Journal of the Food Hygienic Society of Japan 35, 497–503.

Kawashita, S.A., Gamal-el-din, E., Abdalla, M.F., Saleh, N.A.M., 1994. Flavonoids of Plantago species in Egypt. Biochemical Systematics and Ecology 22, 729–733.

Kimura, Y., Okuda, S., Nishibe, S., Arichi, S., 1987. Effects of caffeoylglucosides on arachidonate metabolism in leukocytes. Planta Medica 53, 148–153.

Kyi, K.K., Mya-Bwin, Sein-Gwan, Chit-Maung, Aye-Than, Mya-Tu, M., Tha, S.J., 1971. Hypotensive property of Plantago major Linn. Union of Burma Journal of Life Sciences 4, 167–171.

Larsen, I.M., Olsen, O., Sørensen, H., 1983. Failure to detect glucosinolates in Plantago species. Phytochemistry 22, 2314–2315.

Lawrendiadis, G., 1961. Contribution to the knowledge of the medicinal plants of Greece. Planta Medica 9, 164–169.

Leporatti, M.L., Pavesi, A., 1990. New or uncommon uses of several medicinal plants in some areas of central Italy. Journal of Ethnopharmacology 29, 213–223.

Lim-Sylianco, C.Y., Shier, W.T., 1985. Mutagenic and antimutagenic activities in Philippine medicinal and food plants. Journal of Toxicology — Toxin Reviews 4, 71–105.

Lin, C.C., Shieh, D.E., 1996a. The anti-inflammatory activity of Scutellaria rivularis extracts and its active components, baicalin, baicalein and wogonin. American Journal of Chinese Medicine 24, 31–36.

Lin, C.C., Shieh, D.E., 1996b. In vivo hepatoprotective effect of baicalin, baicain and wogonin from Scutellaria rivularis. Phytotherapy Research 10, 651–654.

Lithander, A., 1992. Intracellular fluid of waybread (Plantago major) as a prophylactic for mammary cancer in mice. Tumor Biology 13, 138–141.

Liu, J., 1995. Pharmacology of oleanolic acid and ursoic acid. Journal of Ethnopharmacology 49, 57–68.

Logan, M.H., 1973. Digestive disorders and plant medicine in highland Guatemala. Anthropos 68, 537–543.

Long, C., Moulis, C., Stanislas, E., Fourasté, É., 1995. L’aucuboside et le catapol dans les feuilles de Plantago lanceolata L., Plantago major L. et Plantago media L. Journal de Pharmacie de Belgique 50, 484–488.

Maksyntina, N.P., 1971a. Baicalin and scutellarein derivatives in the leaves of Plantago major. Chemistry of Natural Compounds 7, 352.

Maksyntina, N.P., 1971b. Hydroxycinnamic acids of Plantago major and Pl. lanceolata, Chemistry of Natural Compounds, 7, 795.

Markov, M., 1992. On the pharmacology of Plantago major. Poster 6 at the 2nd Int. Congr. on Ethnopharmacology, Uppsala, Sweden.

Matsuzaki, Y., Kurokawa, N., Terai, S., Matsumura, Y., Kobayashi, N., Okita, K., 1996. Cell death induced by baicalein in human hepatocellular carcinoma cell lines. Japanese Journal of Cancer Research 87, 170–177.

McCutcheon, A.R., Ellis, S.M., Hancock, R.E.W., Towers, G.H.N., 1992. Antibiotic screening of medicinal plants of the British Columbian native peoples. Journal of Ethnopharmacology 37, 213–223.

McCutcheon, A.R., Ellis, S.M., Hancock, R.E.W., Towers, G.H.N., 1994. Antifungal screening of medicinal plants of British Columbian native peoples. Journal of Ethnopharmacology 44, 157–169.

McCutcheon, A.R., Roberts, T.E., Gibbons, E., et al., 1995. Antiviral screening of British Columbian medicinal plants. Journal of Ethnopharmacology 49, 101–110.

Michaelsen, T.E., Gilje, A., Samuelsen, A.B., Hoegaassen, K., Paulsen, B.S., 1999. Complement activation of a pectin type polysaccharide fraction, PMII from the leaves of Plantago major L., (submitted).

Mironov, V.A., Vasil’ev, G.S., Matrosov, V.S., et al., 1983. Physiologically active alcohols from great plantain. Khimiya-farmatsevticheskii Zhurnal 17, 1321–1325.

Miyase, T., Ishino, M., Akahori, C., Ueno, A., Ohkawa, Y., Tanizawa, H., 1991. Phenylethanoid glycosides from Plantago asiatica. Phytochemistry 30, 2015–2018.

Moongkarn, P., Bunyapraphatsara, N., Srisukh, V., Wagner, H., 1991. The inhibitory activity in 5-lipoxygenase pathway of hispidulin from Millingtonia hortensis Linn. f. Journal of the Science Society of Thailand 17, 51–56.

Morton, J.F., 1975. Current folk remedies of northern Venezuela. Quartery Journal of Crude Drug Research 13, 97–121.

Moscalenko, S.A., 1986. Preliminary screening of far-eastern ethnomedicinal plants for antibacterial activity. Journal of Ethnopharmacology 15, 231–259.

Motoo, Y., Sawabu, N., 1994. Antitumor effects of saikosaponin, baicalin and baicalein on human hepatoma-cell lines. Cancer Letters 86, 91–95.

Murai, M., Tamayama, Y., Nishibe, S., 1995. Phenylethanoids in the herb of Plantago lanceolata and inhibitory effect on arachidonic acid-induced mouse ear edema. Planta Medica 61, 479–480.

Murai, M., Takenaka, T., Nishibe, S., 1996. Iridoids from Plantago major. Natural Medicines 50, 306.

Mølgaard, P., 1986. Population genetics and geographical distribution of caffeic acid esters in leaves of Plantago major in Denmark. Journal of Ecology 74, 1127–1137.

Nagata, K.M., 1971. Hawaiian medicinal plants. Economic Botany 25, 245–254.

Nielsen, H., 1969. Lægeplanter og trolddomsurter. In: Kehler, G.H.N., (Ed.). Politikens Forlag, København, pp. 321-324.

Nishibe, S., Murai, M., Tamayama, Y., 1995. Studies on constituents of plantaginis herba 7: Flavonoids from Plantago asiatica and P. augustifolia. Natural Medicines 49, 340–342.

Nishibe, S., Ono, K., Nakane, H., Kawamura, T., Noro, Y., Tanaka, T., 1997. Studies on constituents of Plantagnis herba 9. Inhibitory effects of flavonoids from Plantago herb on HIV-reverse transcriptase activity. Natural Medicines 51, 547–549.
Noro, Y., Hisata, Y., Okuda, K., et al., 1991. Pharmacognos- 
tical studies of Plantago hinoba (VII) on the phenylethanoid contents of Plantago spp. Japanese Journal of Pharmacognosy 1, 24–28. 
Obolenskova, G.V., Khadzhai, Y.I., 1966. Pharmacological 
study of Plantaglucide (Plantago major leaf extract) used in the treatment of an acid gastritis and peptic ulcer. Farmakologiya i Toksikologiya 29, 469–472 (English abstract). 

tez de Urbina, A.V., Martin, M.L., Fernández, B., San 
Román, L., Cubillo, L., 1994. In vitro antispasmodic activity of peracetylated penstemonoside, aucubin and catapal. Planta Medica 60, 512–515. 
Paller, V.M., Haschke-Hofmeister, E., 1969. Inhalstoffe aus Plantago major. Planta Medica 17, 139–145. 
Pan, P.C., Lay, Y.C., 1966. Application of chinese traditional medicine in the treatment of liver cancer. Zhongyi Zazhi 5, 33–37. 
Ponce-Macotela, M., Navarro-Alegria, L., Matinez-Gordillo, 
M.N., Alvarez-Chacon, R., 1994. In vitro antilardiasic activity of plant extracts. La Revista de Investigación Clinica 46, 343–347. 
Potterson, D., 1983. Culpeper’s Colour Herbal. Sterling Pub-
lishing, New York. 
Qadry, S.M.J.S., 1963. A note on Plantago major seeds: a substitute for ispaghula. Journal of Pharmacy and Phar-
macology 15, 552–555. 
Ramirez, V.R., Mostaers, L.J., García, A.E., et al., 1988. 
Vegetales Empleados en Medicina Tradicional Nopperu-
ana. Banco Agrarian del Peru & NACLI University, Tru-
jillo, Peru, p. 54. 
Rao, R.R., 1981. Ethnobotany of Maghalaya: medicinal plants used by Khasi and Garo tribes. Economic Botany 35, 4–9. 
Rao, R.R., Jamir, N.S., 1982. Ethnobotanical studies in Nagaland. I. Medicinal plants. Economic Botany 36, 176–181. 
Ravn, H., Brimer, L., 1988. Structure and antibacterial activity of plantamajoside, a caffeic acid sugar ester from Plantago major subsp. major. Phytochemistry 27, 3433–3437. 
Ravn, H., Nishibe, S., Sashihara, M., Li, X., 1990. Phenolic compounds from Plantago asiatica. Phytochemistry 29, 3627. 
Recio, M.C., Giner, R.M., Rios, J.L., 1994. Structural consider-
erations on the iridoids as anti-inflammatory agents. Planta Medica 60, 232–234. 
Rice-Evans, C.A., Miller, N.J., Paganga, G., 1996. Structure-
antioxidant activity relationships of flavonoids and phenolic acids. Free Radical Biology and Medicine 20, 933–956. 
Ringbom, T., Segura, L., Noreen, Y., Perera, P., Bolin, L., 1998. Ursolic acid from Plantago major, a selective inhib-
itor of cyclooxygenase-2 catalyzed prostaglandin biosynthesis. Journal of Natural Products 61, 1212–1215. 
Rivera, D., Obón, C., 1995. The ethnopharmacology of Madeira and Porto Santo Islands, a review. Journal of Ethnopharmacology 46, 73–93. 
Roca-Garcia, H., 1972. Weeds: a link with the past. Arnoldia 30, 23–24.
Seaforth, C.E., Ballah, S., Rollocks, S., Craig-James, S., 1998. Medicinal plants used in Tobago. Fitteratropia 69, 523–527.

Selvanayagham, Z.E., Gnanevendhan, S.G., Balakrishna, K., Rao, R.B., 1994. Antisnake venom botanicals from ethnomedicine. Journal of Herbs Spices and Medicinal Plants 2, 45–100.

Shoyama, Y., Matsumoto, M., Nishioka, L., 1987. Phenolic glycosides from diseased roots of Rehmannia glutinosa var. purpurea. Phytochemistry 26, 983–986.

Skari, K.P., Malterud, K.E., Haugli, T., 1999a. Radical scavengers and inhibitors of enzymatic lipid peroxidation from Plantago major, a medicinal plant. In: Kumpulainen, J.T., Salone, J.T. (Eds.), Proceedings of the 2nd International Conference on Natural Antioxidants and Anticarcinogens in Nutrition, Health and Disease. The Royal Society of Chemistry, Cambridge, pp. 200–202.

Skari, K.P., Malterud, K.E., Haugli, T., 1999b. Radical scavengers and inhibitors of enzymatic lipid peroxidation from Plantago major, a medicinal plant. Poster 495 at 2000 Years of Natural Products Research — Past, Present and Future, Amsterdam, The Netherlands.

Smolenski, S.J., Silinis, H., Farinowski, N.R., 1974. Alkaloid Screening. IV. Lloydia 37, 30–61.

Spring, M.A., 1989. Ethnopharmacologic analysis of medicinal plants used by Laotian Hmong refugees in Minnesota. Journal of Ethnopharmacology 26, 65–91.

Suganda, A.G., Amoros, M., Girre, L., 1983. Effets inhibiteurs de quelques extraits bruts et semi purifiés de plantes indigènes françaises sur la multiplication de l’herpesvirus humain 1 et du poliovirus humain 2 en culture cellulaire. Journal of Natural Products 46, 626–632.

Swiatek, K., Kurowska, A., Gora, J., 1980. Chemical composition of some Plantago species seed oil. Herba Polonica 4, 213–217.

Tabata, M., Sezik, E., Honda, G., et al., 1994. Traditional medicine in Turkey III. Folk medicine in east Anatolia, Van and Bitlis. International Journal of Pharmacognosy 32, 3–12.

Taskova, R., Handjieva, N., Evstatieva, L., Popov, S., 1999. Iridoid glucosides from Plantago cornuti, Plantago major and Veronica cymbalaria. Phytochemistry 52, 1443–1445.

Tiwari, K.C., Majumder, R., Bhattacharjee, S., 1979. Folklore medicines from Assam and Arunachal Pradesh (District Tirap). International Journal of Crude Drug Research 17, 61–67.

Toyoda, M., Tanaka, K., Hoshino, K., Akiyama, H., Tanimura, A., Saito, Y., 1997. Profiles of potentially antiallergic flavonoids in 27 kinds of health tea and green tea infusions. Journal of Agricultural and Food Chemistry 45, 2561–2564.

Tutin, T.G., Heywood, V.H., Burges, N.A., et al., 1976. Flora Europaea, vol. 4. Cambridge University Press, Cambridge, p. 39.

Veale, D.J.H., Furman, K.I., Oliver, D.W., 1992. South African traditional herbal medicines used during pregnancy and childbirth. Journal of Ethnopharmacology 36, 185–191.

Wagner, H., 1987. Immunostimulants from higher plants. In: Hostettmann K., Lea P.J. (Eds.), Biologically Active Natural Products. Clarendon press, Oxford.

Wakabayashi, I., 1999. Inhibitory effects of baicalein and wogonin on lipopolysaccharide-induced nitric oxide production in macrophages. Pharmacology and Toxicology 84, 288–291.

Wasuwat, S. (1967). A list of Thai medicinal plants. Research Report No. 1 on Research Project 17, A.S.R.C.T., Bankok, pp. 22.

Weenen, H., Nkunya, M.H.H., Bray, D.H., Mwasumbi, L.B., Kinabo, L.S., Kilimali, V.A.E.B., 1990. Antimalarial activity of Tanzanian medicinal plants. Planta Medica 56, 368–370.

Werenger, B., Rouzier, M., Daguilh, R., Henrys, D., Henrys, J.H., Anton, R., 1986. La médecine populaire dans le plateau central d’Haiti. 2 inventaire ethnopharmacologique. Journal of Ethnopharmacology 17, 13–30.

Xiong, Q.B., Kadota, S., Tani, T., Namba, T., 1996. Antioxidative effects of phytoleutoids from Cistanche deserticola. Biological and Pharmaceutical Bulletin 19, 1580–1585.

Yaremenko, K.V., 1990. Adaptogens of the natural origin in prophylactic oncology. Journal of Cancer Research and Clinical Oncology 116, 82.

Yesilada, E., Sezik, E., Fujita, T., Tanaka, S., Tabata, M., 1993. Screening of some Turkish medicinal plants for their antinociceptive activities. Phytotherapy Research 7, 263–265.

Yesilada, E., Honda, G., Sezik, E., et al., 1995. Traditional medicine in Turkey. V. folk medicine in the inner Taurus Mountains. Journal of Ethnopharmacology 46, 133–152.

Yokozawa, T., Dong, E., Liu, Z.W., Shimizu, M., 1997. Antioxidative activity of flavones and flavonol in vitro. Phytotherapy Research 11, 446–449.

Yoshino, M., Ito, M., Okajima, H., Haneda, M., Murakami, K., 1997. Role of baicalein compounds as antioxidant in the traditional herbal medicine. Biomedical Research—Tokyo 18, 349–352.

You, K.M., Jong, H.G., Kim, H.P., 1999. Inhibition of cyclooxygenase/lipoxygenase from human platelets by polyhydroxylated/methoxylated flavonoids isolated from medicinal plants. Archives of Pharmacal Research 22, 18–24.

Yuting, C., Rongliang, Z., Zhongjian, J., Yong, J., 1990. Flavonoids as superoxide scavengers and antioxidants. Free Radical Biology and Medicine 9, 19–21.

Zagari, A., 1992. Medicinal Plants. Iran Book, Tehran, p. 969

Zennie, T.M., Ogzewalla, C.D., 1977. Ascorbic acid and vitamin A content of edible wild plants of Ohio and Kentucky. Proceedings of the 2nd International Conference on Natural Antioxidants and Anticarcinogens in Nutrition, Health and Disease. The Royal Society of Chemistry, Cambridge, pp. 200–202.