CHAPTER VI

A CASE STUDY OF TURMERIC AND NEEM PATENT REVOCATION AND THEREAFTER

BACKGROUND OF TURMERIC AND NEEM PATENT CASES

The genetic resources and traditional knowledge of India are coming increasingly under the foreign control through the legal mechanism of patents. As a result the legal ownership of the genetic resources is usurped by foreign countries more specifically U.S.A., Germany etc. It is not privatisation of public land but privatisation of public knowledge. Turmeric and neem patents are two examples of this. Turmeric patent is about a product patent and the neem patent is on a process patent. "The revocation of these two cases is significant because on them converged the symbolic fight against appropriation of traditional knowledge made possible by the TRIPs laws. They become the focal point of the assertion of the right of the traditional people over their knowledge rights and their resources. The patent battles came to question the conceptual and moral premises of intellectual property rights which assert the primacy of one kind of knowledge right over another."[1] There are many more instances of bio-pirated patents. It is the Indians who have gifted the knowledge about the neem, turmeric etc to the entire world for the welfare of humankind and other living creatures. Out of magnanimity, the ancient Indians they never tried to obtain patents or other similar monopoly rights to commercially exploit it to the exclusion of all others. The neem tree or the turmeric plant have not been patented, nor have its parts such as leaves, twigs, stems, etc., have been patented. However, certain processes and products which involve various active ingredients of the neem and turmeric have been patented, even though there are documented and non-documented knowledge about them in existence.

PART-I: HALDI (TURMERIC) PATENT RE-EXAMINATION CASE BY USPTO

AN OVERVIEW OF TURMERIC PATENT RE-EXAMINATION CASE

Two US based Indians were granted an US patent 5, 401, 504 by USPTO on March 28, 1995 on "use of turmeric in wound healing." It was a grant of patent on a non-original innovation of turmeric what was actually a part of the public domain traditional knowledge in India. The inventors have claimed that the use of turmeric at the site of an injury by topical application and/or oral intake of turmeric will promote healing of wounds as novel finding and was an inventive step in research. It was

[1] Rajshree Chandra, "Knowledge as Property", in 'Indigenous Knowledge Rights', Oxford University Press, New Delhi, 2010, Page 302.

CSIR, under the leadership of Prof.R.A.Mashelkar that challenged the US patent on for the wound healing properties of turmeric. For any invention, to get the protection of patent has to fulfil the basic requirements of novelty, non-obviousness and utility. But if the claims are described in a printed publication in a foreign country, before the invention thereof and becomes a subject matter of prior art, after the re-examination at different stages, granted patent can also be revoked. Section 102 of 35 U S Code says: a person shall be entitled to a patent unless-(a)the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or (b)the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States. Section 103 of the said code says: A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. CSIR after a painstaking research located 32 references, some of them being more than one hundred years old and in Sanskrit, Urdu and Hindi, which showed that this finding was well known in India prior to filing of this patent. At the first stage, USPTO rejected all the six claims after analysing the 32 references of CSIR about the prior knowledge of wound healing properties of turmeric in India as being "anticipated by the submitted references." After receiving it, the inventors, in the second state, argued that the powder and paste had different physical properties i.e. bio-availability and absorbability and therefore an ordinary skilled person, in the subject would not expect with any reasonable degree of certainty that a powdered material would be useful in the same application as a paste of the same material. At the second stage also USPTO rejected all the claims once again. They made it clear that the paste and the powder forms were "equivalent" for healing wounds in view of the cited prior art. Subsequent to the second rejection, the inventors dropped all their claims and restricted the invention to a "non-healing surgical wound" as supported by the two case histories mentioned in the patent, stating that there was no disclosure or suggestion of using turmeric in surgically inflicted non-healing wounds and requested the examiner to allow the amended claims. But in 1997, the examiner rejected the new claim also as being anticipated as it does not fulfil the criteria of non-obviousness.

The re-examination order of US patent No 5,401,504 on 21st April, 1998 is an epoch making one. By it, an US patent based on the wound healing property of turmeric from the traditional knowledge of India i.e. *method of promoting healing of a wound by administering turmeric to a patient afflicted with the wound,* was revoked and all the claims were cancelled, after a long legal battle. The USPTO revoked this patent in 1997, after ascertaining that there was no novelty; the findings by innovators having been known in India for centuries, no non-obviousness in the claim The judgment not only enthused and worked as a confidence building measure among the dejected and

demoralised Indians but also the entire third world countries whose medicinal plants were robbed through bio-piracy and patented unfairly by the developed countries and generated hopes to get back their intellectual properties. This incident is the starting point to have "no-bio-piracy regime" and "zero tolerance" on bio-piracy, in the world. Although this is a great achievement for India regarding the protection of traditional knowledge of medicinal plants, even under the present legal framework, it is not as if India got back all its traditional knowledge of medicinal plants free from patents. There are umpteen numbers of patents and subsequent commercialisation still exists in so many countries. Little is done, vast undone.

EXTRACTS OF THE WRITTEN SUBMISSION OF THE INVENTORS FOR THE USE OF TURMERIC IN WOUND HEALING, BEFORE THE UNITED STATES PATENT AND TRADEMARK OFFICE, ON WHICH PATENT WAS GRANTED[2]

(a).ABSTRACT-Method of promoting healing of a wound by administering turmeric (curcuma longa) to a patient afflicted with the wound.

(b).BACKGROUND OF THE INVENTION- The active ingredient in turmeric powder is curcumin, which is a completely symmetrical molecule. Curcumin is presumed to be the active moiety; its unique property is its axis of symmetry around the CH2 group. **1.** The present invention relates to the use of turmeric to augment the healing process of chronic and acute wounds. **2.** Principles underlying the healing of chronic ulcers require control of three local factors: infection, oxygenation and edema. The basic process in regard to angiogenesis as it relates to wound healing deals with the capillaries, which consist of endothelial cells and pericytes. These cells do not divide readily but undergo rapid proliferation during spurts of angiogenesis in wound healing. The present inventors have generated experimental evidence showing that turmeric causes endothelial cells to proliferate, indicating that this molecule can be used to augment wound healing. **3.** Althogh it is parimarily a dietary agent, turmeric has been used in India as a traditional medicine for the treatment of various sprains and inflammatory conditions. **4.** Extensive in vitro and in vivo testing has shown that turmeric inhibits chemically-induced epidermal ornithine decarboxylase activity, epidermal DNA synthesis and the promotion of skin tumors in mice. Further studies suggest that turmeric also reduces arachidonic acid-induced rat paw and mouse skin edema and markedly inhibits epidermal lipoxygenase and cyclooxygenase activity in vitro. In humans, ingestion of turmeric has demonstrated a bacteriostatic or bacteriocidal effect against organisms involved in cholecystitis and has been used to treat biliary infections. Topical application of a turmeric paste for the treatment of scabies has also shown good results. **5.** It has been recently shown that curcumin decreased p24 antigen production in acutely or chronically infected cells with HIV-1,

[2] Available at http://www.freepatentsonline.com/5401504.html. Visited on 28 at 28.12.2010 at 7.30 PM. The above extract is written from the original copy of the patent document found in this website.

a paradigm of anti-viral activity. Administration of curcumin in mice significantly reduced the scavenging of peroxides and other activated oxygen species, exhibiting its anti-oxidant property. Oral administration of curcumin in human volunteers has been shown to significantly decrease the level of serum lipid peroxides, increase HDL cholesterol and decrease total serum cholesterol. **6.** The addition of turmeric to diet has been shown to inhibit azoxymethanol-induced colonic epithelial cell proliferation and focal areas of dysplasia. It has also been shown to in interfere with the formation of covalent car-cinogen-DNA adducts. **7.** Fat metabolism is likewise influenced by curcumin. It can render bile non-lithogenic in mice. Curcumin can reduce the production of PMA-induced lipid peroxidation and 8-OH-dexyguanosine formation in mouse fibroblast cells. **8.** Phosphorylation events can also be influenced by curcumin, as it has been reported that curcumin inhibits protein kinase C activity induced by 12-O tetradecanoyl-phorbol-13-acetate in NIH 3T3 cells. **9.** Curcumin inhibits the immume as well as the smooth muscle cell proliferation. Human peripheral blood mononuclear cells were inhibited in response to phyto-hemagglutinin and mixed lymphocyte reaction. Furthermore, curcumin inhibited the proliferation of rabbit vascular smooth muscle cells stimulated by fetal calf serum. Curcumin had a greater inhibitory effect on platelet derived growth factor-stimulated proliferation than on serum-stimulated proliferation. **10.** The anti-inflammatory properties of curcumin were shown to inhibit the 5-lipoxygenase activity in rat peritoneal neutrophils as well as the 12-lypoxyganase and the cyclooxygenase activities in human platelets. Curcumin had no significant effect on quercetin-induced nuclear DNA damage, lipid peroxidation and protein degradation and thus has the unique potential of acting as both pro and anti-oxidants, depending on the redox state of their bio-logical environment.

(c).SUMMARY OF THE INVENTION- The present invention is directed to the use of turmeric to promote wound healing. The present inventors have found that the use of turmeric at the site of an injury by topical application and/or oral intake of turmeric will promote healing of wounds.

(d).DETAILED DESCRIPTION OF THE INVENTION- 1. The present invention provides a method of promoting healing of a wound in a patient, which comprises administering a wound-healing effective amount of tuirmeric to a patient. **2.** The present inventors postulated that turmeric may have significant anti-neoplastic, anti-oxidant, anti-bacterial and anti-inflammatory properties when given orally or applied topically. In view of these facts and the availability of turmeric, the present inventors studied the wound healing properties of turmeric to provide a simple and economical solution to the problem of chronic ulcers. **3.** It is postulated that turmeric contributes to the treatment of chronic ulcers through the following mechanism: (1) improvement of microcirculation, (2) stimulation of angiogenesis, (3) promotion of granulation tissue formation, and (4) acceleration of reepithelialisation. **4.** Some investigators hold that there is no single factor that can address the problem of wound healing. The literature and various conferences stress the use of several growth factors for healing

wounds. This multifactorial approach would result in a very high economic burden on an already strained health care system. Also turmeric is a natural product that is readily available. **5.** Before entering turmeric into a clinical trial, the powder was tested for its healing ability in acute wounds created by surgical incision. The inventors chose to fashion full-thickness circular wounds on rats. All of the wounds in this study exhibited the typical pattern of wound healing with minimum wound contraction noted during the initial lag phase followed by a rapid increase in wound contraction during the proliferation phase (day 6 to day 25). Moreover, the study also suggests that local application and oral intake of turmeric may enhance wound contraction when compared to daily cleansing with saline. **6.** Thus turmeric offers an alternative to conventional therapy for full-thickness wounds. Considering that turmeric is readily available and economical, this could be of particular importance to the indigent population, which suffers significant morbidity from complex wounds.**7.** Growth factor knowledge, the use of animal models and the body of literature on wounds per se have not conclusively addressed the serious problem of skin ulcers. One report detailed an investigation in which two factors, neem and turmeric, were used to treat scabies in a village in India. This multi-drug approach is more difficult to assess than the single factor approach, being used here for humans. Growth factors, in particular platelet derived growth factor and transforming growth factor-B are potential mitogens for epithelialisation as well as fibroblasts. In contrast, in the use of turmeric there is more selectivity with respect to mitogenicity. **8.** Turmeric has been shown to increase HDL in comparison to LDL and hence may also be used in influencing the capillary system by altering the lipid content of blood. Very little of turmeric is systemically absorbed and hence may be working as an advantage by reducing the cholesterol in the blood and hence altering the patency of the vasculature. **9.** The need to address the problem of skin ulcers is apparent. No current animal model, single factor or drug exists. The literature has stressed more on carcinogenic, inflammatory metabolic modulatory or the oxidation properties of turmeric but no one has used this agent singly for wound healing. The present inventors are the first ones to use turmeric topically and orally as a single agent modality for wound healing. **10**. The turmeric can be administered to mammals, including humans, to promote wound healing. Any type of wound on the outside surface of the body can be treated, for example, surgical wounds (such as incisions), ulcers and any other injury to the body in which the skin or other tissue is broken, cut, pierced, torn, etc.

(e).CLAIMS OF THE INVENTORS

1. A method of promoting healing of a wound in a patient, which consists essentially of administering a wound-healing agent consisting of an effective amount of turmeric powder to the patient.

2. The method according to claim1, wherein turmeric is orally administered to the patient.

3. The method according to claim1, wherein turmeric is topically administered to the patient.

4. The method according to claim1, wherein turmeric is both orally and topically administered to the patient.

5. The method according to claim1, wherein the wound is surgical wound.

6. The method according to claim1, wherein the wound is a body ulcer.

(f).RE-EXAMINATION AND REVOCATION OF PATENT ON TURMERIC BY UNITED STATES PATENT AND TRADEMARK OFFICE

CSIR cited and submitted 32 references i.e. Books, Articles etc to show that the wound healing property of turmeric was known to the people in India and it was written in many ancient and modern books and journals. With reference to those printed and published documents, filled the petition for re-examination of the patent aiming at revocation according to 35 U.S.C.301 which states: Any person at any time may cite to the Office in writing prior art consisting of patents or printed publications which that person believes to have a bearing on the patentability of any claim of a particular patent. Hence cannot be considered as 'novel' according to 35 U.S.CODE. 102. which says: A person shall be entitled to a patent unless the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent. There is absence of inventive step in this claim also as what section 103 has said: A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Section 302 of the above Code says that any person at any time may file a request for re-examination by the Office of any claim of a patent on the basis of any prior art cited under the provisions of section 301, which must be in writing. The request must set forth the pertinence and manner of applying cited prior art to every claim for which re-examination is requested. As a result of re-examination of US patent on turmeric, after analysing those documents, it was determined that all the above mentioned claims are cancelled under 35 U.S.C.307. This cancellation or revocation clearly reflects that there was no 'novelty' and 'inventive step'. When the time for appeal was expired, the Director issued and published a certificate cancelling all claims of the patent finally determined to be non-patentable.

(g).CITATION OF PRIOR ART AND REQUEST FOR RE-EXAMINATION VIS-A-VIS REFERENCES WHICH WERE SUBMITTED TO DISPROVE THE CLAIMS OF NOVELTY AND INVENTIVE STEP

With these re-examination grounds and procedural matters in mind CSIR submitted the following list of 32 Articles to disprove the all the claims of novelty and inventive step, to prove that claims are within the ambit of prior art.

1.Gujral et al. Journal of Indian Medical Association, vol. XXII, No.7, pp.273-276, 1953.

2.Frawley, "Ayurvedic Healings", pp.221-223 1989.

3."The Wealth of India", pp 401-405 1950.

4."Indian Materia Medica".pp.414-418 1976.

5."Economic and Medicinal Plant Research", vol. 4, pp.149-151 1990.

6.Sivananda, "Home Remidies", pp. 233-235 1958.

7."The Ayurvedic Pharmacopoeia of India", pp. 45-46 1986.

8."Selected Medicinal Plants of India", p. 56 1992.

9."Indian Medicinal Plants Used in Ayurvedic Preparation", pp. 121-124 1980.

10. Srimal, "Haldi Can Heal", Science Today, pp.26-27 1986.

11. Rastogi et al., "A Compendium of Indian Medicinal Plants", vol. 57, 1985-1989 1993.

12. Ray et al., "Susruta Samhita", p. 62 1980.

13. Amman et al., "Pharmacology of Cuecum Longa", Plant Med. vol. 57, pp. 1-6 1991.

14. Amman et al., "Curcumina: A Potent Inhibitor of Leukotriene B4 Formation" 1992.

15. Srinivas et al., Archives of Biochemistry and Biophysics, vol. 292. No.2, pp. 617-623 Feb. 1, 1991.

16."Dictionary of Indian Folk Medicine and Ethnobotany", pp.65-66 1991.

17. Asolkar et al., Second Supplement to Glossary of Indian medicinal Plants With active Principles Part I (A-K), (1965-1981), pp.246-247 1992.

18. Shalini ey al.,Molecular and Cellular Biochemistry, vol. 95 pp.21-30 1990.

19. Srinivasan et al., Free radical Biology and Medicine, vol. 11,pp. 277-283 1991.

20. Sharma, "Dravyaguna-Vijana vol.II (Vegetable Drugs)", pp. 162-164 1984.

21."Chaukhambha Orientalia", section 332 1979.

22."Rajnighantu of Pandit Narahari", pp. 174-175 1939.

23."Bhavaprakasha", p 115 1969.

24. Sharma, "Ayurveda Ka Vaijnanika Itihasa", p. 187 1975.

25. Chauhan, "Kya Khain Aur kyuon", p. 157 1979.

26. Sattar, " Bustanul Mufredat", p. 157 1979.

27. Satry, "Prayogatmak Abhinav Dravyaguna Vigyanam", pp. 354-356 1991.

28. Kabiruddin, "Makhzanul Mufredat vol. II", pp. 207-208 1955.

29. Khan, "Khazanatul Adviya vol-3", pp. 909-910 1920.

30. Dhawan, Indian Spices, vol. 30, No. 283, 19-20 1993.

31. Reddy et al., 'Indian Medicinal Plants", p. 157 1988.

32. Dey, 'Indian medicinal Plants", p. 157 1988.

(h).COMMENTS OF PROF. R.A.MASHELKAR ON REVOCATION

The grant of patents on non-original innovations (particularly those linked to traditional medicines), which are based on what is already a part of the traditional knowledge of the developing world have been causing a great concern to the developing world. It was CSIR that challenged the US patent No. 5,401,504, which was granted for the wound healing properties of turmeric. This 'second *Haldi Ghati Ladai'*, as it has been referred to, has been a pathbreaking fight for the first time, it asserted the rights of the holders of traditional knowledge from India in international fora.[3] "The turmeric case was a landmark case in that this was the first time that a

[3] "On Building a Golden Triangle between Traditional Medicine, Modern Medicine and Modern Science", speech delivered by R A Mashelkar on 25th May, 2003.

patent based on the traditional knowledge of a developing country was challenged successfully and USPTO revoked the patent. This eventually opened up the path to the creation of Traditional Knowledge Digital Library, Traditional Knowledge Resource Clarification, and finally inclusion of traditional knowledge in the International Patent Clarification System."[4] In the above mentioned speech, Prof. Mashelkar says about the importance IPC: Linking this to internationally accepted International Patent Classification (IPC) System will mean building the bridge between the knowledge contained in an old Sanskrit *Shloka* and the computer screen of a patent examiner in Washington. This will eliminate the problem of the grant of wrong patents, since the Indian rights to that knowledge will be known to the examiner. Hopefully, wrong patents on Turmeric, Neem, etc., will be the things of the past.

PART II: NEEM PATENT REVOCATION CASE BY EPO

AN OVERVIEW OF NEEM PATENT REVOCATION CASE

On 12th December, 1990 W.R. Grace of New York and the United States of America, represented by its Secretary of Agriculture, filed a European Patent Application with the European Patent Office (EPO) on a "method for controlling fungi on plants by the aid of hydrophobic extracted neem oil." After going through the examination procedure, EPO granted European patent, Patent No. 0436257 the main claim having been restricted by the EPO to: "A method for controlling fungi on plants comprising contacting the fungi with a neem oil formulation containing 0.1 to 10% of a hydrophobic extracted neem oil which is substantially free of azadirachtin, 0.005 to 5.0% of emulsifying surfactant, and 0 to 99% water."

A legal opposition to this patent was filed jointly by Dr. Vandana Shiva, on behalf of the Research Foundation for Science, Technology and National Resource Policy, New Delhi, India; Magda Aelvoet, MEP, the then President of the Green Group in the European Parliament, Brussels; and Linda Bullard, Vice President of the International Federation of Organic Agriculture Movements, based in Germany. The petitioners claimed that the fungicidal effect of hydrophobic extracts of neem seeds was known and used for centuries on a broad scale in India, both in Ayurvedic medicine to cure dermatological diseases, and in traditional Indian agricultural practice to protect crops from being destroyed by fungal infections. Since this traditional Indian knowledge was in fact ubiquitous in Indian culture from ancient times, they asserted that the patent in question lacked two basic statutory requirements for the grant of a European

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Available at
http://www.csir.res.in/External/Heads/aboutcsir/leaders/DG/DG%20speech%201.htm. Visited on 21st June, 2011, at 4.15 PM.

[4] R. A. Mashelkar, "Intellectual Property Rights and the Third World" Vol.7, No.4, Journal of Intellectual Property Rights, Pp 308-323, July 2002.

patent, namely "novelty" as per Article 54, EPC and "inventive step" according to Article 56, EPC. The petitioners also contended that the patent was contrary to "morality," according to Article 53 (a) of the EPC. This is because the inventors claimed monopolistic property rights on a method which forms part of the traditional knowledge base of India. In essence it is an act of stealing and stealing or theft is regarded as immoral and unethical in European culture. Lastly, they cited the formal grounds of "insufficient disclosure" under Article 83, EPC and "lack of clarity" under Article 84, EPC to justify the revocation of the patent. Subsequently, they also requested for an additional reason to oppose the patent that it constituted *de facto* monopoly on a single plant variety, which is not allowed under Article 53 (b), EPC.
To substantiate their contentions, the petitioners brought two expert witnesses from India: Dr. Udai Pratap Singh, Professor and Head Department of Mycology and Plant Pathology, Institute of Agricultural Sciences, BHU and Mr. Abhay Dattaray Phadke of Puna-Managing Director of Ajay Bio-Tech (India) Ltd. Dr. Singh is widely regarded as India's greatest expert on neem in the scientific community. Mr. Phadke is an agronomist and had commercialized a neem product in India, without claiming patent protection. The patentees adopted the tactics to attack the petition on procedural grounds. However, the Opposition Division supported the petitioners on all the procedural questions.

First Dr. A. D. Phadke was called. His presentation was lengthy, detailed, with excellent documentation and absolutely crushing and convincing. At the end of his oral and written testimony, the panel opined that the patentee's claim of novelty had been negatived by the presence of clearly demonstrated prior public use. Soon after, the lawyers Grace and USA submitted an "auxiliary request" by amending neem formulation slightly to keep it outside the described parameters and also to protect the patent from being cancelled. After immediate examination of the amended claim, the Opposition Division ruled that amended form of the "invention" was lacking an inventive step.
The Opposition Division did not accept the arguments that the patent constituted a *de facto* monopoly on a single plant variety or that it was a violation of "public order and morality." But the members of OD agreed with the arguments of the petitioners that no patents should be granted for anything which was known previously, for example as part of common traditional knowledge. However, under the EPC this is not a matter under Article 53(a) EPC, but is a question of novelty or prior public use.
On 13 February 2001 Opposition division of EPO revoked European patent No. 0436257 i.e. method for controlling fungi on plants by the aid of a hydrophobic extracted neem oil. The detailed cross examination and verifying the submitted documents proved beyond doubt to the Opposition Division that the patent was based on pirated knowledge. Having aggrieved to this revocation, W.R. Grace and the United States of America as represented by its Secretary of Agriculture, appealed to the next level within the EPO, Technical Board of Appeal, demanding that the decision of the Opposition Division be overturned and submitting yet another modified formulation of their original claim. Although two days had been set aside to

examine the Appeal, the case was so compelling that the five-member Technical Board of Appeals needed only two hours to reach its decision. It had earlier declined to hear Mr. Phadke again, or Dr. Singh, although the work of both was referred to during the proceedings. The patentees had renewed their attempts to have the case declared inadmissible on procedural grounds, but the panel did not even discuss these questions. A second "auxiliary request" amending the formula of the product was refused on the grounds that it enlarged the scope according to Article 123(2). Then the main body of the patent was examined with regard to novelty, disclosure, and inventive step in the light of written submissions and oral presentations. 8th March 2005, is a historic and ever memorable day in the fight against bio-piracy. EPO revoked in its entirety a patent on a fungicide made from seeds of the neem tree, concluding a ten-year battle in the world's first legal challenge to a biopiracy patent. The TBA did not explain the grounds for its decision. But it analysed and considered the decision of Opposition Division of EPO in its judgment. It can be said that the ratio of the Opposition Division's decision was upheld.

WRITTEN SUBMISSION OF THE INVENTORS OF THE INVENTER ON METHOD FOR CONTROLLING FUNGI ON PLANTS BY THE AID OF HYDROPHOBIC NEEM OIL BEFORE EPOON WHICH PATENT WAS GRANTED EARLIER[5]

(a).DESCRIPTION OF THE INVENTION

This invention relates to a method of controlling fungi on plants with the aid of a foliar fungicide comprising a hydrophobic-solvent extracted neem oil. These neem oil pesticides exhibit inter alia the ability to prevent fungal growth and kill fungal pests at various life stages.

(b).CLAIMS OF THE INVERTOR

1. A method of controlling fungi on plants comprising contacting the fungi with a neem oil formulation containing 0.1 to 10% of a hydrophobic extracted neem oil which is substantially free of azadirachtin, 0.005 to 5.0% of emulsifying surfactant and 0 to 99% water. 2. The method according to Claim 1 wherein the neem oil formulation contains 0.25 to 3% neem oil. 3. The method according to Claim 1 wherein the fungi are selected from the group consisting of mildews, rusts, leaf spots, dollar spots, brown patch and botrytis. 4. The method of claim 1 wherein the fungi is contacted with the neem oil formulation on the surface of the plants. 5. The method of claim 4 wherein the fungi is contacted with the neem oil formulation by spraying. 6. The method of claim 1 wherein the plants are turf, horticultural or agricultural crops.

[5] Available at http://www.freepatentsonline.com/0436257.html. Visited on 28th December, 2010, at 7.30 PM.

7. A method for protecting a plant from fungi infestation comprising contacting the plant with a neem oil formulation containing 0.1 to 10 of a hydrophobic extracted neem oil which is substantially free of azadirachtin, 0.005 to 5.0% of emulsifying surfactant and 0 to 99% of water. 8. The method of Claim 7 wherein the plant is contacted with the neem oil formulation by spraying. 9. The method of Claim 7 wherein the plants are turf, horticultural or agricultural crops. 10. The method of Claim 7 wherein the plant is contacted with a fungicidally effective amount of the neem formulation.

(c).DESCRIPTION OF PRIOR ART

The neem tree, a tropical evergreen, has been used for centuries as a source of pesticides to which insects have not developed a resistance. Various neem seed extracts, particularly the ones containing the hydrophilic, tetranortriterpenoid azadirachtin, are known to influence the feeding behavior, metamorphosis, fecundity, and fitness of numerous insect species belonging to various orders.

It is known that neem oil, containing azadirachtin, may be mechanically pressed from neem seeds in the cold by using oil presses or may be extracted using alcohols or other solvents using Soxhlet apparatus. Small amounts of neem oil can be obtained by kneading neem seed powder by hand after adding some water. Thus the term 'neem oil' has been used to describe a variety of materials containing a mixture of both hydrophilic and hydrophobic extractables.

The variety of extraction methods and resultant variety in composition of neem oil has led to great confusion as to the true properties of "neem oil". Khan and Wassilew, Proc. 3rd Int. Neem Conf., 645-650 (1986) tested the effect of their "neem oil" (prepared by aqueous extraction of neem kernels) on 14 common fungi, including Trichophytonrubrum , T. violaceus, T. concentrichus, T. mentagrophytes , Enidermophyton floccosum , Mierosporum citaneum, Scrophulariopsis brevicaulis , Geotrichum candidum and Fusarium sp and found that it did not inhibit fungal growth and, in fact, the neem oil itself actually contained several species of growing fungi. Yet an anonymous article reported that "10% Neem oil diluted from its emulsifiable concentrate formulation" completely inhibited several species of fungi such as Aspergillus niger , Fusarium moniliforme , Macrophomina phaseolina and Drechslera rostrata . However, the specific details of this formulation were not provided.

Similarly, there are discrepencies in the literature as to the use of neem oil to control insects. Schmutterer and Hallpap, Vol. 1: The Neem Tree, "Effects of Neem on Pests of Vegetable and Fruit Trees", 69-83 (1986) showed that aqueous neem seed extracts are significantly superior to neem oil in repelling leaf mites (Scrobipalpa ergasina), leaf roller (Phycita melogenu) and leaf hopper (Jacobiella facialna). While Mansour et al., Proc. 3rd Int. Neem Conf., 577-587, Nairobi (1986) report that the pentane extract of neem seeds was much more effective at controlling the spider mite

Tetranychus cinnabarinus than were ethanol or methanol extracts, but surprisingly, the pentane extract was less effective at controlling the mite, Phytoseiulus persimilis than were the ethanol or methanol extracts.

Yamasaki, et al, Journal of Chromatography, Vol. 447, 277-283 (1988), showed that the tetranortriterpenoid, salannin, can be isolated from crude plant extracts, obtained from Indian neem seeds which are known to be high in salannin content, using hexane. The biological activity of the salannin extract is reported to be feeding deterency and growth inhibition when applied to chewing insects such as beetles and caterpillers.

From Entomology Experimentalis et Applicata, vol. 24, no. 3, 1978, pages 448-450 it is known to use a neem seed extract produced by extraction with hexane. The crude hexane extract of the neem seed is crystallized from an acetone solution, filtered and freed from solvent under reduced pressure and is reported to have insecticidal properties as repellant, reduction of egg deposition. This extract may be used in an aqueous emulsion containing 0.2% Tween 20 ^{R} as surfactant.

From Phytoparasitica, vol. 11, no. 3/4, 1983, pages 177-185 it is known to use chloroform and pentane extracts of neem seed against carmine spider mite (repellency, reduction of fecundity of adult females). The neem seed is extracted with pentane or chloroform, the resultant mixture is filtered and finally the solvents are evaporated.

However, the use of the neem oil extract (extracted by a non-polar solvent) as foliar fungicide is neither disclosed in the state of the art nor is it derivable therefrom although the principle fungicidal effect of neem seed is known from the state of the art (Biological Abstracts, vol. 71, no. 12, 1987, abstract no. 83379).

It has now been discovered that under the process of this invention, a non-polar hydrophobic-solvent extracted neem oil, substantially free of azadirachtin, possesses the ability to control the growth of serious fungal pathogens. This activity as fungicide in the absence of azadirachtin is novel and unique. The fungicidal activities of hydrophobicly extracted neem oil is unique and unexpected in view of the absence of any known active ingredients.

(d).SUMMARY OF THE INVENTION

It is an object of this invention to provide a novel pesticide that controls the growth of various fungi. Another object of this invention is to provide a natural pesticide formulation derived from neem seed extracts for the protection of plants from various fungal pests. To reach the objects of the invention there is suggested the method according to claims 1 to 6.

In accordance with the present invention, there have been provided certain novel pesticide formulations derived from seed extracts, said formulations comprising non-polar hydrophobic-solvent extracted neem oil fractions that are substantially free of azadirachtin and salannin.

(e).DETAILED DESCRIPTION

Some active ingredients of the seeds and leaves of the tropical neem tree, Azadirachtin indica, particularly the tetranortriterpenoids azadirachtin and salannin, are known for their potent pesticidal activities. The present invention is directed to various pesticide formulations prepared from neem oil which are substantially free of azadirachtin, and yet said formulations possess the ability to control fungal pathogens.

Neem seeds can be quite variable in size, shape and composition. Seeds from around the world can be as small and round as a pea and as large and long as a bean. Neem seeds consist of two parts, a shell that does not contain oil or pesticidal activity and the kernal which contains oil and azadirachtin. However, the composition of seeds collected from throughout the world varies considerably as shown in Table A. In particular we have found that oil derived from neem trees with high azadirachtin concentration is fungicidal.

The pesticide formulations of this invention are prepared from neem oil which has been extracted from, dried, coarsely ground neem seeds with a suitable non-polar, hydrophobic solvent. In accordance with this invention, dried neem seeds, typically containing about 5 to 15% water, are coarsely ground to about 4 mm sieve opening (5 mesh). The ground neem seeds are then extracted with a non-polar hydrophobic solvent to remove neem oil. It is preferred to use a significant excess of solvent (3 to 1 w/w) to obtain good yields. The solvent must be suitably hydrophobic to prevent excess water from contaminating the product. Water in the extract will cause azadirachtin to be extracted from the seeds and result in hydrolysis of the extract. After extraction, the solvent is removed from the extract by low temperature evaporation, preferably by vacuum evaporation to yield the neem oil product.

Final pesticide formulations, in accordance with this invention, can be prepared by diluting the neem oil with about 5 to 50% preferably 5 to 20% and most preferably 7 to 15% by volume emulsifying surfactant and may optionally contain 0-1% PABA. Suitable emulsifying surfactants include sorbitan esters, ethoxylated and propoxylated mono and diglycerides, acetylated mono- or diglycerides, lactylated mono- or diglycerides, citric acid esters of mono- or diglycerides, sugar esters, polysorbates, poly-glycerol esters, and the like, and mixtures thereof. The preferred emulsifying surfactants are the polyoxyethylene derivatives of fatty acid partial esters of sorbital anhydrides which are sold under the name Tween® 20, Tween® 40, Tween® 60 and Tween® 80. Prior to final application, these pesticide formulations are typically diluted with water.

For foliar application it has been observed that rates of 0.1 to 10%, preferably 0.25 to 3% neem oil diluted in water is effective for control of insect pests and fungal diseases without unacceptable plant damage. Neem oil may also be used at various dilutions to control various pest and disease problems on turf, horticultural and agricultural crops as well as stored fruits and vegetables. The neem oil formulations have been shown to be effective at controlling fungi such as mildews, rusts, dollar spot, brown patch, black spots, botrytis, and the like.

Suitable non-polar, hydrophobic solvents for use in extracting the neem oil from the ground neem seeds will include those solvents having high neem oil solubility and substantially no azadirachtin or water solubility. The preferred non-polar solvents include, but are not limited to, aliphatic hydrocarbons and halogenated aliphatic hydrocarbons such as pentane, hexane, heptane, octane, nonane, decane, isooctane, chloropentane, chlorohexane, and the like, and their isomers; petroleum distillates, petroleum ether, and the like; aromatics and substituted aromatics such as benzene, toluene, chlorobenzene, benzaldehyde, xylenes, and the like; and mixtures thereof. Various other non-polar solvents having the above characteristics are well known to those skilled in the art, and the choice of a particular solvent is not per se critical to the invention, provided that it is substantially azadirachtin-insoluble and neem oil has a high degree of solubility therein.

(f).EXAMPLE-I

This example illustrates the effectiveness of the non-polar, hydrophobic-solvent extracted neem oil formulations of this invention on the Control of Bean Rust   Neem oil was extracted according to the following procedure.

Eighty (80) kgs of dried defruited neem seeds from Africa were ground in a cutting mill to about 2 mm seive opening (10 mesh). The ground seeds were added to a 300 gallon (1136.&litre) agitated vessel together with 140 gallons (529 &litre) of hexane and agitated for 18 hours. The extracted seeds were then separated from the hexane-neem oil solution by centrifugation. The hexane-neem oil solution was transferred to a 500 ml jacketed agitated vessel where the solution was heated to 165°F (74°C) to remove the excess hexane. The recovered neem oil had a hexane content of 1%.

The extracted neem oil was mixed with water and diluted to 0.25, 0.5, and 1% and sprayed on the fully expanded primary leaves of beans cv. Pinto 111 until run off. The leaves were then inoculated with bean rust (Uromyces phaseoli) spores and placed in a dew chamber to allow infection. After approximately 16 hours the bean plants were removed from the dew chamber and placed in a greenhouse. After seven (7) days the number of rust pustules were counted. The results, in Table 4, show that the extracted neem oil is an effective foliar fungicide at these concentrations.

(g).EXAMPLE-II

Control of Mildew on Hydrangea

A solution of 2% extracted neem oil in water was sprayed on 5 hydrangias plants growing in greenhouse. The treated plants and an equal number of untreated plants were exposed to the natural mildew microrganisms found in the greenhouse for 6 weeks. At the end of this period the leaves of the plants were examined for mildew infestion. The untreated plants had an average of 46% of their leaves infested while the treated plants had 1.7% infestation.

(h).DECISION OF THE TECHNICAL BOARD OF APPEAL OF EPO-REVOCATION OF NEEM PATENT[6]

Decision under appeal: Decision of the Opposition Division of the European Patent Office posted 13 February 2001 revoking European patent No. 0436257 pursuant to Article 102(1) EPC.

SUMMARY OF FACTS AND SUBMISSIONS

I. European patent No. 0 436 257 based on application No. 90 250 319.2 was granted on the basis of ten claims.

Independent claim 1 as granted reads as follows:

"1. A method of controlling fungi on plants comprising contacting the fungi with a neem oil formulation containing 0.1 to 10% of a hydrophobic extracted neem oil which is substantially free of azadirachtin, 0.005 to 5.0% of emulsifying surfactant and 0 to 99% water."

II. The following documents and pieces of evidence *interalia* were cited in the proceedings:

(8) H. B. Singh and U. P. Singh, Australian Plant Pathology, pages 66 to 67, 1981.

A2 Affidavit of Mr A. D. Phadke of 27 August 1996

A7 Affidavit of Mr A. D. Phadke of 14 May 1998

A10 Affidavit of Prof. U. P. Singh of 8 January 1998

A13 Affidavit of Mr A. D. Phadke of 19 November 2003

Testimony of Mr A. D. Phadke before the opposition division (minutes of the taking of evidence by hearing the witness Mr A. D. Phadke recorded in the oral proceedings before the opposition division on 9 May 2000, closed on 10 May 2000).

III. Opposition was filed and revocation of the patent in its entirety was requested pursuant to Article 100(a) EPC on the grounds of lack of novelty (Article 54(1) and (2) EPC, lack of inventive step (Article 56 EPC) and because the invention would be contrary to morality (Article 53(a) EPC) and pursuant to Article 100(b) EPC on the

[6] Available at http://www.freepatentsonline.com/0436257.pdf. Visited on 7th June, 2011, at 4.21PM.

grounds of insufficiency of disclosure. The ground concerning Article 53(b) EPC was introduced later on during the opposition proceedings.

IV. The appeal lies from a decision of the opposition division revoking the patent under Article 102(1) EPC. The opposition division considered the opposition to be admissible.

The opposition division considered the requirements of sufficiency of disclosure (Article 83 EPC) to be met since the description contained enough information to perform the invention by choosing one hydrophobic solvent among the list of possible solvents and the result of the extraction was a product substantially azadirachtin-free. With respect to Article 53(a) and (b) EPC, the opposition division stated that in the present case *inter alia* the question raised in respect of the traditional knowledge was a question of state of the art for assessment of novelty since the patent did not give its proprietor any right to prohibit acts in India. Moreover, no plant variety was claimed but a method of controlling fungi by a hydrophobic extract of the oil from seeds of a generically defined tree. Additionally, the opposition division further stated that the extract used in the claimed method was obtainable from seeds of Azadirachta indica (neem tree), but this was a plant species, i.e. a higher taxonomic unit than a plant variety. The opposition division considered the public prior use to be proven on the basis of affidavit A7 by Mr A.D. Phadke together with his testimony during the oral proceedings before the opposition division. In particular, the opposition division considered that the "when" and "where" of the alleged prior use were clearly established as summer 1985 and 1986 in the Pune and Sangli districts of Maharashtra, Western India. The fungicidal effect was observed in the months of November and December. In particular, Mr Phadke himself had carried out some of the tests with two farmers.

The opposition division also considered that the testimony established the following: that hydrophobic extract (with a non-polar hydrophobic solvent such as hexane) from neem seeds was diluted with an emulsifying surfactant (either synthetic such as TweenR or natural such as Acida Consica); that the products used were compositions containing less than 1% hexane, 90% neem oil and 10% emulsifier (synthetic) or 85% neem oil and 15% emulsifier (natural) and that for pest control 4-8 ml of the above product were diluted in 1l water resulting in a final concentration of about 0.4-0.8% neem oil (0.36-0.72%) and about 0.04-0.08% emulsifier.In the opposition division's view the witness made clear that the broader values mentioned in affidavit A7, namely 0.5-5% of neem oil, concerned the whole period, whereas the specific concentration 0.4-0.8% was applied in the first year.

The opposition division was of the opinion that both the testimony and affidavit A7 confirmed the treatment of agricultural crops such as rice, lentils or sunflowers and of fruits and vegetables such as grapes, tomatoes, strawberries, mangoes and pomegranates and beans. The target was insects and diseases caused by fungi such as powdery mildew, rust, brown patches, black spots and botrytis. An unlimited number of local farmers could take note of said treatment.

Additionally, since the extraction with hexane was also made in example 1 of the patent in suit, the opposition division considered that the hexane extracts were substantially free of azadirachtin as a consequence of the choice of the solvent used for the extraction. According to the opposition division's findings the main request (claims as granted) lacked novelty and the auxiliary request (filed during the oral proceedings before the opposition division) lacked an inventive step. With respect to inventive step, the opposition division considered that the prior use represented the closest prior art. It defined the problem to be solved as finding alternative methods for controlling fungi or protecting plants. In the opposition division's view the skilled person would have used formulations comprising a lower concentration of the neem oil extract as obvious lower cost alternatives of the known formulations.

V. The appellant (patentee) lodged an appeal against the decision.

VI. The respondents (opponents) filed counterarguments.

VII. The board sent a communication on 6 June 2003 expressing rapporteur's preliminary comments in respect of the admissibility of the opposition, as well as some objections within the meaning of Article 123(2) EPC concerning the auxiliary request.

VIII. The respondents filed further arguments and *inter alia* a further affidavit A13 by Mr A.D. Phadke.

IX. The appellant filed an amended set of claims with its letter of 16 February 2004.

Claim 1 of the auxiliary request read as follows:

"1. A method of controlling fungi on plants comprising contacting the fungi by way of foliar application with a neem oil formulation containing 0.25% of a neem oil obtainable by extraction of neem seeds with a non-polar hydrophobic solvent by way of adding dried and ground neem seeds to the solvent and agitating same, which neem oil is substantially free of azadirachtin and salannin, 0.005 to 5.0% of emulsifying surfactant and up to 99% water."

X. In a communication sent on 17 August 2004 as an annex to the invitation to oral proceedings, the board mentioned document (8) as relevant for the assessment of inventive step.

XI. The respondents filed more arguments dealing with several aspects of the case. In particular they objected to claim 1 of the auxiliary request under Article 123(2) EPC.

XII. In a letter of 24 November 2004 the appellant announced that it would not be attending the oral proceedings and that it withdrew its request for oral proceedings.

XIII. The board sent a communication on 9 December 2004 expressing the preliminary opinion that claims 1 and 5 of the auxiliary request did not meet the requirements of Article 123(2) EPC.

XIV. Oral proceedings were held before the board on 8 March 2005.

XV. The appellant's arguments were filed in writing with the grounds of appeal. They may be summarised as follows:

The opposition was not admissible since three opponents paid one opposition fee and filed and signed one opposition letter without being represented by a professional European representative. It was questionable whether the one opposition fee paid was

indeed paid in time since a bank account sheet in the official file bore the date of the last day of the opposition period and stated "Receipt of payment to another account". If the opposition fee was paid on the last possible day by transfer order from one account to another, it was very unlikely that it reached the receiving account on the very same day.

The opponents needed a representative for the opposition to be deemed filed, and this applied at least to the non-European opponent. The representative was appointed later, i.e. after the opposition time limit had expired. The opposition as originally filed was insufficiently supported by facts and arguments with respect to the several grounds for opposition cited therein. Additionally, it was immediately clear from the beginning that the objection raised in the original opposition letter with respect to morality did not apply to the claimed subject-matter. The prior use was not sufficiently proven. In particular, the appellant considered that Mr Phadke relied on documentation (such as laboratory books), in order to refresh his knowledge when giving his affidavits and testimony, which was not introduced into the proceedings. Therefore, the appellant could not verify the contents of these documents. Furthermore, Mr Phadke did not identify in the opposition proceedings before the first instance one individual local farmer. Since about 10 to 14 years had passed since the alleged action, it had to be taken into account that for most people the recollection of dates and numerals was not reliable and hence supporting documents were needed. It was furthermore unproven whether the alleged tests had actually been carried out and in particular what specifically had been tested or demonstrated and to whom. To that extent there was insufficient evidence to decide against the novelty of the claimed subject-matter.

The appellant also stated in its grounds of appeal that since the opposition division determined the prior use based on Mr Phadke's affidavits and testimony to be the closest prior art there was also an insufficient basis and support for the decision of lack of inventive step. Additionally, reference was made with respect to the further arguments in the opposition's proceedings concerning inventive step.

The appellant also requested remittal to the first instance for further prosecution in case the main request was found to be novel by the board, since the inventive step of the main request had not been discussed during the oral proceedings before the first instance. No further arguments were submitted by the appellant in response to the board's communications.

XVI. The respondents stated during the oral proceedings that in view of the board's communications and the board's preliminary comment it would concentrate its arguments as follows:

With respect to the main request there was an insufficient disclosure and the subject-matter claimed lacked novelty and inventive step. As support for its arguments, the respondents cited affidavits A2, A7, A10, A13, the testimony of A. D. Phadke and document (8).

As regards the requirements of Article 83 EPC, the respondents considered that the process parameters (temperature, time of extraction, agitation mode) necessary for performing the extraction were not sufficiently disclosed. With respect to the novelty analysis, it referred to affidavits A2, A7 and to Mr A. D. Phadke's testimony.

The respondents shared the conclusions reached by the opposition division in its decision. All the features appearing in claim 1 were anticipated by the prior use supported by Mr A. D. Phadke's statutory declarations and testimony. The respondent further stressed that the feature "substantially free of azadirachtin" was redundant, since it was a direct result of the extraction with a hydrophobic solvent.
With respect to inventive step, the respondents considered either the prior use as closest prior art or, alternatively, document (8). In the respondents' view the skilled person faced with the problem of finding an alternative to the known method of controlling fungi referred to in the prior use would have immediately arrived at the claimed invention. With respect to the auxiliary request the respondents considered that it did not meet the requirements of Article 123(2) EPC.
In particular, amended claim 1 related to a combination of specific features which were not disclosed in such a way in the original application. The contents of the patent application should not be taken as a reservoir from which it would be permissible to draw features pertaining to separate embodiments in order to create artificially a particular embodiment, which was now claimed. It cited decision T 305/87, Official Journal EPO, 1991, 429. The respondent stated that it shared the board's preliminary opinion expressed in the communication of 9 December 2004 with respect to the process features "adding dried and ground neem seeds to the solvent and agitating same". Furthermore, if example 1 was the basis for the amendments, then an unallowable generalisation had also taken place with respect to the temperature of the extraction. In example 1 the extraction took place at room temperature, whereas the extraction temperature was not mentioned in the claim. Hence the claim also encompassed the possibility of heating.
XVII. The appellant (patentee) had requested in writing that the decision under appeal be set aside and that the patent be maintained as granted (main request) or, as auxiliary request, that the patent be maintained in amended form on the basis of the set of claims filed with letter dated 16.02.2004.
The respondents (opponents) requested that the appeal be dismissed.

REASONS FOR THE DECISION

1. The appeal is admissible.
2. *Admissibility of the opposition*
The matter of the admissibility of the opposition concerning the payment of only one opposition fee for an opposition filed in common by two or more persons has been answered by decision G 003/99, OJ EPO 2002, 347.
Point 1 of the Order in G 003/99 reads as follows: "1. An opposition filed in common by two or more persons, which otherwise meets the requirements of Article 99 EPC and Rules 1 and 55 EPC, is admissible on payment of only one opposition fee." Therefore the payment of only one opposition fee is not questionable in the present case. With respect to the question arising in connection with the date of payment of the opposition fee (Article 99(1) EPC and Article 8(1)(a) of the Rules relating to Fees)

in due time, the respondents alleged that the fee was paid cash to the European Patent Office's account on 14 June 1995 (last day).
In the opposition's file, the said date is to be seen in the "receipt payment to another account" from Banque Bruxelles Lambert in Bruxells. In the said receipt, the European Patent Office appears as "Beneficiary". In view of this evidence of payment, this date can be considered as the date on which the payment was made. Moreover, even if assuming, as asserted by the appellant, that a debit order in respect of a payment from one account to another was made instead of cash payment to the EPO's account, a situation was created in which the payment to the EPO's account could not be revoked or changed by the remitter, either as regards the date or the amount (cf. T 214/83, OJ EPO, 1985, pages 10 to 14, especially point 4).
With respect to the appointment of a professional representative in accordance with Article 133(2) EPC,this requirement only applied to the second opponent, but not to the first and third opponents. This is because the first and third opponents had a residence or their principal place of business within the territory of one of the Contracting States (Belgium and Germany respectively). Accordingly, even if the appellant's position was to be confirmed in respect of the second opponent, the admissibility of the opposition for the first and third opponents cannot be challenged.
With respect to the point raised by the appellant in relation to a possible insufficiency of the grounds for the opposition, it has to be distinguished between the case where the opposition was accompanied with sufficient reasons, as is the case here, and the case where the reasons given were likely to lead to a revocation of the contested patent. The latter being a substantive matter, the formal requirement of Article 99(1) EPC is met anyway. Accordingly, the opposition is admissible since it meets the requirements of Article 99 EPC and Rules 1 and 55 EPC and it is in conformity with the conclusions reached in G 003/99.
3. With respect to the appellant's request for remittal to the department of first instance, it has to be remembered that the board has the discretionary power to decide on the remittal to the first instance (Article 111(1) EPC) after consideration of the merits of each case. There is no absolute right to two instances in the sense of a party being in all circumstances entitled to have every aspect of its case examined by two instances. In the present case, considering the overall length of the opposition and appeal proceedings, remitting the case to the department of first instance is not justified since this would impair the legitimate interests of the other party and of the general public in having some degree of legal certainty as to the existence and scope of the European patent within a reasonable time span.
The oral proceedings before the board took place in the absence of the appellant who was duly summoned but decided not to attend, as announced with its letter of 24 November 2004. The present decision is based on facts and evidence put forward during the written proceedings. Therefore, the conditions set forth in decision G 004/92 (OJ EPO 1994, 149) are met in the present case.
4. *Main request*
4.1. Sufficiency of disclosure

When considering whether the requirements of sufficiency of disclosure are met, the contents of the whole patent have to be investigated in the light of the general knowledge in the field. The board shares the opposition division's opinion that the description contains enough information to perform the invention. Moreover, the respondents have not contested the reproducibility of example 1. The respondents have objected that the process parameters for the extraction were not sufficiently disclosed. However, even if the description does not go deeply into the details of the extraction process, the skilled person may use its general knowledge to supplement the information contained in the patent. The person skilled in the art means the skilled person who is expected to have the same qualifications as the relevant skilled person referred to under Article 56 EPC for assessing inventive step. In the present case it is the skilled person working in the field of plant fungicides with technical general knowledge on natural products. The board is convinced that in order to carry out the invention as claimed in the main request the skilled person does not require anything other than the contents of the description, including example 1, and routine experimentation based on her or his general knowledge. In conclusion, the requirements of Article 83 EPC are met.

4.2. State of the art

To prove the alleged public prior use, the respondents put forward affidavits A2, A7, A13 and the testimony of Mr A. D. Phadke. The appellant has disputed the validity of the evidence brought forward *inter alia* on the grounds that it casts doubt on the credibility of the evidence. This doubt was based on the long period which had elapsed between the actions and the affidavits and testimony. The appellant's main argument was that the recollection of dates and numerals was uncertain for most people and hence some supporting documents, such as laboratory books or notebooks, were required. However, there is no dispute between the parties concerning the existence of the prior art document (8) as part of the state of the art within the meaning of Article 54(2) EPC. In the board's view, document (8) is highly relevant for the ruling of the present case. Thus, it can beleft open whether or not the prior use is proven as the case can be decided on the basis of document (8) alone.

4.3. Novelty

Although document (8) discloses the use of an extract of neem oil as fungicidal on plants, it does not disclose which is the solvent employed. Moreover, document (8) does not disclose the presence of an emulsifying surfactant in the formulations employed. Therefore the subject-matter claimed is novel over the contents of document (8).

4.4. Inventive step

Document (8) represents the closest prior art. This document relates to a scientific publication on the "Effect of Volatiles of Some Plant Extracts and their Oils on Conidia of *Erysiphe polygoni* DC." (cf. title). "The present study reports the effect of volatiles of garlic extract and oil, **neem oil** and ginger (*Zingiber officinale* Rosc.) rhizome extract on conidia of powdery mildew (*Erysiphe polygoni* DC) of pea (*pleum sativum* L.)." (*emphasis added*) (cf. end of first paragraph in the left-hand column on page 66). Document (8) also refers to the known antifungal activity of neem extracts

and oil. "Extracts and oils of garlic (*Allium sativum* L.) and neem (*Azadirachta indica* Juss.) exhibit strong antifungal activity but their antifungal effect has not been studied so far on powdery mildews." (cf. first paragraph in the lefthand column on page 66). The neem oil used in document (8) is an extracted neem oil, since it was obtained "by Soxhlet apparatus" (cf. end of second paragraph in the left-hand column on page 66). Moreover, for the tests performed disclosed in document (8) "Freshly produced mature conidia of *E. polygoni* were dusted onto cover glasses from pea plants raised in the greenhouse" (cf. third paragraph in the lefthand column on page 66).

Different concentrations of oils were used according to document (8). Specific values for neem oil are shown on Table 1 in the right-hand column of page 66. These values are expressed as ppm (v/v) (cf. third paragraph in the left-hand column on page 66) and correspond to 0.01, 0.05, 0.1, 0.2, 0.3 and 0.5% respectively. Document (8) further discloses that neem oil exhibited a marked inhibitory effect on spore germination and germ tube length. (cf. first paragraph in the righthand column on page 66).

Document (8) also discloses that "The results of the present experiments reveal that the volatiles of oils and extracts of plant parts mentioned above have strong antifungal effect at relatively low concentrations **in vitro**. This prompted us to include them in our spraying program in the field for the control of powdery mildew of pea where ginger extract has given excellent results; studies on other oils and extracts are still in progress." (cf. second paragraph in the right-hand column on page 66).

In the light of this prior art, the problem underlying the patent in suit can be defined as putting into practice a method of controlling fungi on plants by using an extracted neem oil. The problem is solved by the features of claim 1 "contacting the fungi with a neem oil formulation containing 0.1 to 10% of a hydrophobic extracted neem oil which is substantially free of azadirachtin, 0.005 to 5.0% of emulsifying surfactant."

Having regard to examples 1 and 2 in the description of the contested patent, the board is satisfied that the problem has been plausibly solved. It remains to be investigated whether the proposed solution is obvious to the skilled person in the light of the prior art. Although not explicitly mentioned in document (8), it has not been disputed that the neem seeds are the source for obtaining the extracted neem oil. Additionally, claim 1 of the main request does not specify this feature.

The skilled person faced with the problem defined above knows that she or he has to put in contact the fungi with formulations containing neem oil in some concentration. This is an obvious requirement of the known methods of controlling fungi on plants. Mildews are among the fungi to be controlled which are mentioned in the description of the patent in suit (cf. page 4, line 57). Since document (8) specifies that the neem oil used is a neem oil obtained by Soxhlet apparatus the use of a solvent for the extraction is compulsory. However, document (8) does not disclose which solvent should be used. Accordingly, the skilled person would use his or her general knowledge of the isolation of natural products from plants. This commonly takes place by means of solvent extraction and solvent elution. These are well-known practices used in all laboratories of natural products and merely imply arranging the solvents to be used according to their solvent strength.

Basically, whatever the technique chosen, it is normally started with a non-polar hydrophobic solvent (first option) and then it is continued in increasing degree of polarity up to hydrophilic solvents (waterincluded). Since the method disclosed in document (8) is solvent extraction (by using a Soxhlet apparatus), the skilled person uses that method and would begin with a hydrophobic solvent. In this context it has to be remembered that the claim does not specify the temperature of the extraction and hence extraction by Soxhlet apparatus is also encompassed by the claim wording.

As regards the concentrations of extracted neem oil to be used in the formulation suitable for the antifungal effect, the specific concentrations disclosed in document (8) clearly fall within the scope of claim 1 (0.1 to 10%).

With respect to the fact that an emulsifying surfactant is present in the formulation in a concentration of 0.005 to 0.5%, this is a usual measure when commonly providing formulations from hydrophobic plant extracts. Moreover, the appellant has not alleged that any effect is achieved derived from the use of the surfactant in this specific range other than its usual function as additive for providing formulations suitable for use as pesticides in general.

It is a fact acknowledged by the appellant in the patent description that such formulations are known *per se* (page 3, lines 41 to 45, of the patent in suit). Since the claimed subject-matter comprises formulations with water contents of **0%** it is not necessary to comment on this aspect.

As regards the feature "which is substantially free of azadirachtin", this is a direct result of the hydrophobic extraction, since azadirachtin is a tetranortriterpenoid produced by the neem tree which is not soluble in hydrophobic solvents such as hydrocarbons (e.g. hexane). This is confirmed by the fact that example 1 of the patent in suit does not require any process step in addition to the extraction with hexane.

Consequently, the subject-matter of claim 1 of the main request lacks an inventive step since it was obvious to try to use formulations such as those defined in the claim for controlling fungi on plants. Although the patentee was aware (board's communication sent as an annex to the summons for oral proceedings) that the board considered document (8) as relevant for the assessment of inventive step, it chose not to file any arguments in support of an inventive step for the claimed subject-matter.

The only argument on file with respect to document (8) can be seen in the minutes of the oral proceedings before the opposition division, where the appellant discards document (8) by stating without further reasoning that this document does not mention a hydrophobic solvent. This argument is an argument related to the novelty of the claim. Moreover, as set out above, the use of a hydrophobic extract derives from the systematic routine of laboratory work. In conclusion, the main request fails for lack of inventive step (Article 56 EPC).

5. *Auxiliary request*

5.1. Article 123(2) EPC Claim 1 of the first auxiliary request contains the feature "by way of adding dried and ground neem seeds to the solvent and agitating same". There are two passages in the application as originally filed which disclose the preparation of the neem oil by way of extraction: page 6, lines 10 to 26, and example 1, page 9, lines 2 to 8. None of these passages reflects identically the text appearing in the

claims. The passage on page 6 (lines 12, 13) discloses that the neem oil is extracted from dried, coarsely ground neem seeds (emphasis added) and states nothing about agitation. It is further stated on page 6 that "In accordance with this invention, dried neem seeds, typically containing about 5 to 15% water, are coarsely ground to about 5 mesh. The ground neem seeds are then extracted with a non-polar hydrophobic solvent to remove neem oil" (emphasis added). Additionally, example 1 of the application as filed relates to specific conditions for the extraction with a specific solvent, namely: "Eighty (80) kgs of dried defruited neem seeds from Africa were ground in a cutting mill to about 10 mesh. The ground seeds were added to a 300 gallon agitated vessel together with 140 gallons (259 kgs) of hexane and agitated for 18 hours. The extracted seeds were then separated from the hexaneneem oil solution by centrifugation. The hexane-neem oil solution was transferred to a 500 ml jacketed agitated vessel where the solution was heated to 165°F [74°C] to remove the excess hexane." (emphasis added). Therefore, the amendments mentioned above relate to unallowable generalisations of features of the application as originally filed (Article 123(2) EPC). The patentee has not filed any counterarguments. Consequently, the auxiliary request fails since it does not meet the requirements of Article 123(2) EPC.

ORDER

For these reasons it is decided that: The appeal is dismissed.

SOME OBSERVATIONS OF THE ACTIVISTS ABOUT NEEM BATTLE

Linda Bullard, former president of International Federation of Organic Agriculture Movements, Germany said about one of her reasons to fight against EPO patent on neem with Vandana Shiva and others. She says; "They wished to illuminate how governments of wealthy countries—in this case the United States—and multinational corporations—in this case the infamous W.R. Grace (whose exploits are chronicled in the book and movie "A Civil Action")—collude to steal biological resources from the south by means of the patent system."[7] She also says: "It is important to note that the case was won on the basis of affidavits and testimony, and that the intellectual achievements of traditional societies were recognized officially as a means to establish "prior use".[8]

Vandana Shiva of Research Foundation for Science, Technology and National Resource Policy, India gives some valuable observations about the value of neem together with the significance of the battle against neem patent. "Neem is an extremely important social and cultural symbol in Indian society because it is used on such a large scale for medicine and agriculture in India. If biopiracy can occur with

[7] FREEING THE FREE TREE, A BRIEFING PAPER ON THE FIRST LEGAL DEFEAT OF A BIPIRACY PATENT: The Neem Case, by Linda , Bullard, March 2005. Available at http://www.nwrage.org/content/freeing-free-tree-briefing-paper-neem-biopiracy-case. Visited on 23rd March, 2009, at 11.46 AM.

[8] Ibid.

such commonly used knowledge, what would be the fate of less prevalent examples of traditional innovation? Neem is also important because it is an ecologically sound alternative to hazardous pesticides." "The neem battle is a contest between eco-feminism and capitalist patriarchy. Eco-feminism recognises the intrinsic worth and integrity of all beings, including all the various species and different kinds of people and societies, while capitalist patriarchy recognises only the rights of those who own and control capital, which happens to be largely men. The rights of capital and the rights of privileged and powerful men reinforce each other and create unjust and unethical systems like Western style IPR regimes which attempt to transform all life and living resources under the monopoly of corporations. Freeing the free tree was an experiment. It sought to find new ways to defend our freedoms in an era of globalisation and corporate rule".[9] In her book "The Plunder of Nature and Knowledge" to respond to W.R Grace's justification for patents which hinges on the claim that their modernised extraction processes constitute a genuine innovation, Vandana Shiva says that "this novelty, however exists mainly in the context of the ignorance of the West. Over 2000 years that neem-based bio-pesticides and medicines have been used in India, many complex processes were developed to make them available for specific use, though the active ingredients were not given Latinised scientific names."[10] She continues to say that "Biodiversity has different properties that can be utilised for meeting human needs. In the case of neem, the knowledge that the tree has biopesticidal properties is metaknowledge-the knowledge of principles-in the public domain. Given this knowledge, various processes of technology can be used for preparing a variety of products from neem. These are obvious, not novel."[11]

PART-III: NEEM PATENT RE-EXAMINATION CASE BY USPTO

AN OVERVIEW OF NEEM PATENT RE-EXAMINATION CASE

W R Grace's U S neem patent, Patent No. 5, 124, 349 for 'storage-stable pesticide formulations containing azadirachtin as the active ingredient' has sparked a sharp and spontaneous furore among all Indians-farmers, scientists, jurists, civil society members, social activists etc. It is a patent for the pesticide composition containing neem seed extracts and characterised by non-degrading solvent system. This patent was a traditional knowledge based, gives an exclusive right to the product was the cause of so many concerns. One concern was that the patent will deprive local farmers of their ability and privilege to produce and use neem-based pesticides by altering the price and availability of the neem seeds. This is the reason why they were up in arms against this traditional knowledge based patent. In the mean time, on a related matter of this patent, Grace also was granted a patent from EPO. This patent was challenged

[9] Available at http://www.gene.ch/genet/2000/Jun/msg00032.html. Visited on 5th June,2011 at 6.35 PM.
[10] Dr. Vandana Shiva, "Biopiracy: The Plunder of Nature and Knowledge", in 'Biodiversity and People's Knowledge', RFSTE, New Delhi, 1997, Page-71.
[11] Ibid, Page 71.

before EPO and was revoked subsequently. The initiative to move for challenge was initiated by Jeremy Rifkin from The Foundation on Economic Trends in the US; Dr Vandana Shiva, President of The Research Foundation for Science, Technology and Natural Resource Policy in India; Dr M D Nanjundaswamy of Karnataka Rajya Ryota Sangha, a farm organisation representing farmers throughout India; Linda Bullard, the then Vice-President of the International Federation of Organic Agriculture Movements in Brussels, Germany; and Martin Khor, Director of the Third World Network.

The challenge is based on the ground that the pesticidal extract in question has long been known to the Indians for thousands of years and was used by them for protecting their crops to resist the attack of the pests and insects as well. It was derived from the knowledge and use that lay in the public domain as the formulation was developed and used by Indian farmers. Therefore the knowledge of this was therefore available at the time of patenting, to any ordinary person and the difference between it and the patented product, if any, was 'obvious', hence not an inventive step. But there have been no efforts to patent most of these inventions because Indian patent law forbids agricultural and medicinal products.

IT IS BARRED BY PRIOR ART

Under Sections 301 and 302 of the 35 US Code, any individual may file a request for the re-examination of an existing patent if the requester believes 'prior art' would have a bearing on the patentability of any claim of the patent. It includes knowledge that was available at the time of patenting to a person of ordinary skill in the art. This patent should be overturned because the company's method of extracting stable compounds has been widely used prior to the patent's issuance and because the extraction methods have been previously described in printed publications.

Several centuries of learning, research, creativity and experimentation with the neem have resulted in a wealth of information on how to harness the tree's potential for use in medicine, agriculture etc. It is the accumulation of centuries' old Indian knowledge. The accumulated knowledge is the result of many anonymous and individual efforts carried out over hundreds of years. This patent is about a "process" of extracting stable chemical compounds for use in pesticides. Yet, Indian villagers have been extracting the tree's chemical for pesticidal uses via similar processes for several centuries. People at the village level have developed several ways of extracting and in fact been extracting by similar processes for centuries the neem's pesticidal emulsions without expensive equipment. They break down the seeds and soak them overnight in water, alcohol or other solvents years ahead of company's patented processes. The emulsions float to the surface and are then placed directly on crops as a pesticide and insect repellent. Need was not felt to store pesticidal compositions because they usually apply the emulsions the following day. Despite the simplicity of these traditional methods, the pesticidal compounds obtained are

extremely effective. Moreover, these compounds are just as potent as pesticides derived from more sophisticated methods. Several studies have demonstrated that compounds derived from these traditional methods are as successful in warding off pests as synthetic insecticides. These traditional methods of chemical extraction are especially useful in long-term pest control. While insects become tolerant to single chemicals, these indigenous methods yield complex blends of compounds. This blending makes it much less likely that insects will become tolerant to the extract's toxicity.

This prior use is well documented. It can invalidate the claim of novelty. Although patented process is more technical, it is merely extension of the same processes that Indian villagers have been using for hundreds of years. Patents cannot be granted for trivial or minor changes or an obvious extension of prior art. to known products and processes. In addition to this prior use, Indian researchers documented the use of the seed's compounds as a pesticide over 50 years ago. There are extensive research works of some modern scientists on the use of the neem as a pesticide in India. First reported case is in the year 1928. Two Indian scientists, R N Chopera and M A Husain, reported using neem tree kernels to repel desert locusts. In 1962 field test by M Pradhan shows that when ground up neem kernels were mixed with water, the resulting suspended compound served as an effective pesticide and neem kernels are even more potent than industrial insecticides. Moreover, some Indian research has studied the production of stable neem-based solutions and emulsions. Indian scientists made significant advances in the field of neem-oriented stabilisation techniques in the 1960s and 1970s. Additionally, the Indian Agricultural Research Institute conducted formal scientific studies of the neem tree, demonstrating the effectiveness of neem tree seeds in pesticides and insect repellents over a decade ahead of the patentee's earliest efforts. This pre-existing body of knowledge and research of Indian scientists renders the patent claims invalid. It does not matter whether the patentee had actual knowledge i.e. prior art, of its existence. Patentee is to be held accountable.

THE CLAIMS ARE NOT OF ANY INVENTIVE STEP

The issuance of a patent is prohibited if the patent would have been an 'obvious' in light of prior art. The standard for patentability requires that the differences between a patentable invention and its prior art must be great enough so that a person with ordinary skill in the art would not consider the invention to be obvious at the time of patenting. This patent does not meet this standard.

The patent is non-obvious in nature and characteristics. This claim is based on the reason that in contrast to the traditional chemical extraction techniques, the patented process obtains storage-stable azadirachtin formulations. It has several flaws. Firstly, several Indian scientists had developed stabilisation techniques prior to Grace's patent application. So whatever was made out by Grace, there was nothing non-obvious in it. It could have very easily anticipated by those persons who developed these techniques

or other ordinarily skilled persons in that technique. Secondly, in determining whether an invention is obvious, it is necessary to consider the possibilities and capabilities of pre-existing technologies. Inventions are unpatentable if the possibilities raised by prior technologies would make the patent obvious to a person with ordinary skill in the art. This standard also disqualifies the validity. Because Indian researchers had already developed the knowledge and technology necessary to make storage-stable azadirachtin formulations possible, this pre-existing knowledge subsumes Grace's patent claims. Patents may not be granted for trivial changes to known products and processes.

Grace tries to prove by saying that claim is non-obvious because there are no pre-existing references identical to patent processes. His emphasis is that there has to have some specific formal references identifying storage-stable azadirachtin formulations. This argument fails for two reasons. First, it is obvious that indigenous village traditions would not be recorded in formal publications. To expect Indian villagers to formally publish centuries-old learned traditions is unrealistic and unfair. By citing a lack of formal publications as proof of non-obviousness, it holds the villagers to a standard that is clearly unobtainable. Second, it is immaterial that no reference makes the same specific claims of the patented process because the proper test is to be determined from combined teachings of prior references. Rather than seeking specific patents or publications that mirror Grace's claims, a proper examination of prior art should conduct a broad and interpretive analysis of all prior references. Considering: that Indian villagers developed neem-based pesticides years before Grace obtained its patent; that scientists from around the world documented the effectiveness of the neem tree in pest control prior to Grace and that Indian scientists initiated and developed the research on stable neem compounds. A new use of the same knowledge does not justify exclusive patent rights. A patent monopoly should not be granted on trivial improvements which are new, but obvious modifications of known products and processes.

But the arguments were rejected by USPTO and it confirmed all the 19 claims.

EXTRACTS OF THE PATENT APPLICATION OF THE INVENTOR-W.R.GRACE BEFORE THE UNITED STATES PATENT AND TRADEMARK OFFICE ON WHICH PATENT NO. 5, 124,349 WAS GRANTED

(a).FIELD OF THE INVENTION

This invention relates to pesticide compositions, and more specifically to storage-stable pesticide formulations containing azadirachtin as the active ingredient.

(b).BACKGROUND OF THE INVENTION

The biological activities of the neem tree seeds have long been recognized. Of primary importance are the potent pesticidal properties of azadirachtin, the main active ingredient in the neem seed. Azadirachtin is a tetranortriterpenoid that causes feeding inhibition and growth disruption in various insect, mite, nematode, etc. orders.

There are various methods known in the prior art to extract azadirachtin from neem seeds, including the use of solvents such as methanol, ethanol, water, methylene chloride, chloroform, hexane, methylethylketone, butanol, petroleum benzene, ether, acetone, methyl tertbutyl ether, diethylcarbonate, etc. In general, it has been found that the efficiency of the extract yield can be increased by increasing the solvent polarity, i.e.,- from hexane to ethanol, ethanol to methanol, methanol to water, etc. However, while various studies have examined relative solvent extraction efficiencies, little attention has focused on the shelf life stability of azadirachtin in solution.

The most significant limitation to the successful use of azadirachtin as a pesticide and insect repellant is the ability of the azadirachtin in solution. One study has shown that heat and sunlight (UV radiation) cause rapid degradation of azadirachtin. J. Environ. Sci. Health, A17(1), 57-65 (1982) by J. B. Stokes and R. E. Redfern. Sunlight degradation of azadirachtin can be effectively reduced by addition of UV absorbing additives such as para-aminobenzoic acid (PABA), neem oil, angelica oil, castor oil, or calmus oil. Other factors known to affect the storage stability of azadirachtin are the concentration of azadirachtin in solution and the pH of the solution. U.S.Patent. No. 4,556,562 discloses improvement in storage properties of azadirachtin in aqueous ethanol emulsions by adjusting the concentration of azadirachtin in the range 2000 to 4000 ppm and adjusting the pH in the range 3.5 to 6.0. It now has been discovered that the stability of azadirachtin in solution is decreased in the presence of protic solvents, in particular water, acids and bases.

(c).SUMMARY OF THE INVENTION

The object of this invention to provide a non-toxic, natural pesticide formulation based on an extract from neem seeds with improved storage stability; to provide a process for preparing storage stable azadirachtin formulations wherein the formulation is characterized by its non-degrading solvent system and to provide a storage stable neem seed extract formulation having azadirachtin as the active pesticidal ingredient wherein the formulation is characterized by incorporating solvents which are non-degrading toward azadirachtin. In accordance with the present invention, there have been provided certain novel pesticide formulations containing azadirachtin as an active ingredient, said formulations characterized by the particular non-degrading nature of the solvent system with respect to azadirachtin. As used herein, the term non-degrading relates to aprotic solvents that do not cause the

decomposition of azadirachtin in solution. The aprotic solvents of this invention are characterized by the absence of any acidic or basic functionalities. The azadirachtin formulations of this invention, by virtue of their non-degrading solvent systems, offer improved shelf life stability over the prior art ethanol-water based formulations.

(d).DETAILED DESCRIPTION

The present invention is directed to storage stable azadirachtin compositions which have been formulated using non-degrading solvent systems. As used herein, the term "storage stable" refers to formulations that have retained at least 80% of their active ingredient content after one year at room temperature (25° C.). It has now been discovered that the stability of azadirachtin is substantially decreased by the presence of protic solvents, in particular those solvents having acidic or basic functional groups specifically water, acids and bases. There are basically two non-degrading solvent systems acceptable for use in the azadirachtin formulations of the invention, namely alcohols and "aprotic" solvents. In accordance with the present invention, azadirachtin formulations with enhanced stability are obtained when the solvent system of the formulation is comprised of either greater than 50% by volume alcoholic solvents containing less than 5% water, or greater than 50% by volume aprotic solvents containing less than 15% water. The compositions covered in this application contain one or more surfactants in total concentration of at least about 1.0%, up to 10%.

Aprotic solvents are defined as polar solvents having moderately high dielectric constants, which do not contain acidic hydrogen, Morrison and Boyd, Organic Chemistry 3rd. Edition, 31 (1974). The various factors that determine whether a given solvent is protic or aprotic are only qualitatively understood. The proton donating or proton accepting interaction is usually greatest when the atom attached to the proton is nitrogen or oxygen. This behavior has been attributed to hydrogen bonding. In general, the hydrogen bond strength increases with increasing acidity of the proton-donating group, and increasing basicity of the proton-accepting group. Aprotic solvents suitable for use in this invention will be those solvents that do not contain acidic or basic functional groups and do not degrade into acids or bases, including, but not limited to, ketones, nitriles, substituted aromatics such as alkyl or halogenated aromatics, amides, sulfoxides, alkyl carbonates, chlorinated aliphatics, aromatic aldehydes, sulfones, ethers, esters, and the like, or mixtures thereof. The preferred aprotic solvents for use in this invention include, but are not limited to, acetone, 2-butanone, 3-methyl-2-butanone, cyclohexanone, acetonitrile, xylenes, chlorobenzene, methylene chloride, chloroform trichloroethane, ethylene chloride benzaldehyde, sulfolane, methyl-t-butyl ether, dibutyl ether, ethyl acetate, propyl acetate, amyl acetate, dimethylsulfoxide (DMSO), dimethylformamide (DMF), dimethylacetamide, diethylcarbonate, propylene carbonate, ethylene carbonate, and mixtures thereof. Various other solvents having the above aprotic characteristics are known to those skilled in the art, and the choice of a particular solvent is not per se critical to the invention, provided that azadirachtin has a high degree of solubility therein, and the

solvent does not cause degradation of the azadirachtin by proton donating or proton accepting interactions.

Suitable alcoholic solvents for use in this invention include, but are not limited to, methanol, ethanol, propanol, isopropanol, butanol, 2-butanol, t-butanol, benzyl alcohol, and the like, and mixtures thereof.

Solvents which are unacceptable for use in the solvent systems of this invention are those protic solvents characterized by the presence of acidic or basic functional groups which can undergo proton-transfer reactions that result in charged species such as $RCOO^-$ or RNH_3^+. Those solvents known to degrade azadirachtin include bases such as amines or hydroxides, acids such as mineral acids or carboxylic acids. However, the final azadirachtin formulations of this invention may contain minor amounts of these solvents, typically less than 1% by volume for the control of pH and the like.

The storage stable azadirachtin formulations of this invention can be prepared by either of two general procedures.

A first embodiment of this invention is to extract azadirachtin and neem oil together from dried neem seeds that have been coarsely ground to about 5 mesh. The ground neem seeds are extracted by using a polar solvent having azadirachtin solubility. If desired, the polar solvent extraction may be repeated to optimize the extraction efficiency.

Because dried neem seeds retain between 6 and 15% water, this polar solvent extraction, in addition to extracting azadirachtin, also extracts a significant amount of water. The neem seed extracts typically contain about 20% by volume water. Since water is an azadirachtin-degrading, protic solvent, its presence in neem seed extracts above the previously defined allowable limits will reduce the storage stability of the azadirachtin formulations. It has been discovered that the allowable limit to the amount of water in a neem seed extract is dependent upon the aprotic/protic character of the particular solvent system of the extract. Specifically, if the solvent system is comprised of greater than 50% by volume aprotic solvents such as ketones or esters, the concentration of water must be less than 15% by volume of the total solution. Alternatively, if the solvent system comprises greater than 50% alcohol solvents, (which are more protic) the concentration of water must be less than 5%, preferably less than 2%, and most preferably less than 1% by volume of the total solution.

There are various techniques to reduce the concentration of water in the final solutions to within the above defined acceptable limits including, but not limited to, further extracting the neem seed extracts with a water-immiscible solvent, diluting the extracts with an appropriate aprotic solvent, or drying the extracts over a suitable adsorbent.

A preferred embodiment of this invention is to extract dried neem seeds that have been milled to a coarse powder of about 5 mesh with a non-polar, azadirachtin-insoluble aprotic solvent such as hexane to remove the neem oil from the seeds. This "cleanup" extraction is then followed by a second extraction of the defatted neem seeds using a more polar, azadirachtin-soluble solvent. As in the first embodiment, this extraction may be repeated to optimize the extraction efficiency. .

The final azadirachtin pesticide formulations of this invention preferably contain at least about 1.0 up to 10% emulsifying surfactant, 0 to 40% neem oil, 0 to 1% para-aminobenzoic acid or its esters, and less than 1% acetic acid or sodium hydroxide to adjust the pH to between about 3.8 and 4.2

(e).CLAIMS OF THE INVENTERS

(1). A storage-stable pesticide composition comprising a neem seed extract solution containing azadirachtin wherein the solution has at least 50% by volume aprotic solvent, at least about 1.0% but less than 10% surfactant, and less than 15% by volume water, said solution being non-degrading to azadirachtin. (2). A storage-stable pesticide composition according to claim 1 wherein the aprotic solvent is selected from the group consisting of nitriles, substituted aromatics, chlorinated aliphatics, aromatic aldehydes, sulfones, ethers, esters, amides, sulfoxides, alkyl carbonates, ketones, and mixtures thereof. (3). A storage stable pesticide composition according to claim 1 wherein the solution further includes 0 to 40% neem oil, 0 to 1 percent para-aminobenzoic acid or its esters, and the pH is adjusted to between 3.8 and 4.2 with the addition of sodium hydroxide or acetic acid, wherein the percentages are on weight/weight basis. (4). A storage-stable pesticide composition comprising neem seed extract solution containing azadirachtin wherein the solution has at least 50% by volume alcohol solvent, at least about 1.0% but less than 10% surfactant, and less than 5% by volume water, said solution being non-degrading to azadirachtin. (5). A storage-stable pesticide composition according to claim 4 wherein the solution has at least 50% by volume alcohol solvent and less than 2% by volume water. (6). A storage-stable pesticide composition according to claim 4 wherein the solution has at least 50% by volume alcohol solvent and less than 1% by volume water. (7). A storage stable pesticide composition according to claim 4 wherein the alcohol solvent is selected from the group consisting of methanol, ethanol, propanol, isopropanol, butanol, 2-butanol, t-butanol, benzyl alcohol and mixtures thereof. (8). A storage stable pesticide composition according to claim 4 the solution further includes 0 to 40% neem oil, 0 to 1 percent para-aminobenzoic acid or its esters, and the pH is adjusted to between 3.8 and 4.2 with the addition of sodium hydroxide or acetic acid, wherein the percentage are on a weight/ weight basis. (9). A process for the preparation of a storage-stable pesticide composition comprising the steps of: (a) extracting neem oil from coarsely ground neem seeds with a non-polar azadirachtin-insoluble aprotic solvent, (b) extracting azadirachtin from the defatted neem seeds with a polar aprotic solvent, and (c) adjusting the azadirachtin extract from (b) by

diluting with additional aprotic solvents or further extracting with a water-immiscible aprotic solvent to obtain a storage-stable pesticide composition having greater than 50% by volume aprotic solvent, at least about 1.0% but less than 10% surfactant, and less than 15% by volume water.

10. A process according to claim 9 wherein the aprotic solvent is selected from the group consisting of ketones, nitriles, substituted aromatics, chlorinated aliphatics, aromatic aldehydes, sulfones, ethers, esters, amides, sulfoxides, alkyl carbonates and mixtures thereof. (11). A process for the preparation of a storage-stable pesticide composition comprising the steps of: a. extracting neem oil from coarsely ground neem seeds with a non-polar azadirachtin-insoluble aprotic solvent, b. extracting azadirachtin from the defatted neem seeds with a alcohol solvent, and c. adjusting the azadirachtin extract from (b) by either diluting or further extracting with a water-immiscible aprotic solvent to obtain a storage-stable pesticide composition having greater than 50% by volume alcohol solvent, at least about 1.0% but less than 10% surfactant, and less than
5% by volume water. (12). A process according to claim 11 wherein the composition has at least 50% by volume alcohol solvent and less than 2% by volume water. (13). A process according to claim 11 wherein the composition has at least 50% by volume alcohol solvent and less than 1% by volume water. (14). A process according to claim 11 wherein the alcohol solvent is selected from the group consisting of methanol, ethanol, propanol, isopropanol, butanol, 2-butanol, t-butanol, benzyl alcohol and mixtures thereof. (15). A process for the preparation of a storage-stable pesticide composition comprising the steps of: a. extracting azadirachtin and neem oil from coarsely ground neem seeds with a polar aprotic solvent, and b. adjusting the azadirachtin extract from (a) by either diluting or further extracting with a water-immiscible aprotic solvent to obtain a storage-stable pesticide composition has greater than 50% by volume aprotic solvent, at least about 1.0% but less than 10% surfactant, and less than 15% by volume water. (16). A process according to claim 15 wherein the polar aprotic solvent is selected from the group consisting of ketones, nitriles, substituted aromatics, chlorinated aliphatics, aromatic aldehydes, sulfones, ethers, esters, amides, sulfoxides,
Alkyl carbones and mixtures thereof. (17). A process for the preparation of a storage-stable pesticide composition comprising the steps of: a. extracting azadirachtin and neem oil from coarsely ground neem seeds with an alcohol solvent, and b. adjusting the azadirachtin extract from (a) by either diluting or further extracting with a water-immiscible aprotic solvent to obtain a storage-stable pesticide composition having greater than 50% by volume alcohol solvent, at least about 1.0% but less than 10% surfactant, and less than 5% by volume water. (18). A process according to claim 17 wherein the composition has at least 50% by volume alcohol solvent and less than 2% by volume water. (19). A process according to claim 17 wherein the composition has at least 50% by volume alcohol solvent and less than 1% by volume water.

SOME OBSERVATIONS REGARDINF THE FAILED NEEM BATTLE

It is really disappointing to know that Grace neem patent was revoked by the EPO but a related patent was upheld by the USPTO. Margo A Bagley says in one of his brilliant research papers that "Section 102's geographical limitation is particularly problematic with respect to public knowledge or use of inventions in developing countries. The neem tree controversy provides a fitting example of the types of problems the limitation engenders."[12] He continues to say that "Why was one Grace neem patent revoked by EPO while a related patent was upheld by USPTO? One of the culprits may have been Section 102's geographical limitation on prior art. Evidence of foreign use of the invention that was key to the revocation of the European patent would not be admissible to challenge the validity of any related U.S.patent on neem because of the geographical limitation on prior art codified in various subsections of S 102 of the Patent Act of 1952. In a nutshell, S 102 excludes evidence of foreign public knowledge or use of an invention from being considered in both novelty and non-obviousness determinations if the evidence is not contained in a patent or printed publication."[13] Section 102 says: *A person shall be entitled to a patent unless-(a)the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or (b)the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States.* There is no evidentiary value of prior public use of the process or product in a foreign country in the eyes of US patent law. That is why the arguments were flatly rejected by USPTO. As it was a process, the printed documents about neems medicinal or agricultural values did not have any bearing on the patentability criterion.

Attacking the claims of novelty, Vandana Shiva asserted that the theory that azadirachtin was being destroyed during traditional processing is inaccurate.[14] She is also of the view that the extracts were subject to degradation, but that was not the problem, because the product was used within a few days of production by Indian farmers. Therefore, there was no immediate need for a process of stabilizing the extract. The need for extract preservation only arises in case of mass production for broader and distinct export markets. Moreover, she added that stabilisation techniques had already been developed by Indian scientists in 1960s. Margosam-O is a simple

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[12] Margo A Bagley, Patently Unconstitutional: The Geographical Limitation on prior art in a Small World, MINNESOTA LAW REVIEW (Vol 87.679) Page 680. Available at http://heinonline.org. Visited on 12th June 2011 at 5.35 PM.

[13] Ibid, Pages 682-683.

[14] Vandana Shiva, The Neem Tree-A Case History of Biopiracy, Thirld World Network. Available at http://www.twnside.org.sg/title/pir-ch.htm. Visited on 24th April, 2009, at 10.30 AM.

ethanolic extract of neem seed kernel.[15] Existing neem patent applies only to methods of extracting the natural chemical in the form of a stable emulsion or solution; this is simply an extension of the traditional process for making neem-based product. The discovery of neem's pesticidal properties and its process was thus 'obvious' and minor derivative that is 'obvious'.

AND AFTER.....

NEED, FUNCTION AND IMPORTANCE OF THE ESTABLISHMENT OF TRADITIONAL KNOWLEDGE DIGITAL LIBRARY (TKDL)

Traditional Knowledge Digital Library (TKDL) is established by Central Scientific Research Laboratory (CSIR). It is really a very positive and concrete work done by the then Government Of India through CSIR, that's effect is being felt today and would be felt in future, not only in India but also in foreign countries. It is a documentation of the written descriptions of India's traditional knowledge associated with medicinal plants from the ancient Indian books written in various languages. This is to give detailed and required informations regarding the medicinal values of the Indian plants to the whole world for the first time. This digitised documentation is according to the systems of western world and TRIPs legal framework. This manner and method these countries follow while searching prior art at the time of patent application consideration and at the time of revocation processes. India did not have such complete and comprehensive documentation of prior art about the medicinal properties of plants. So India suffered a lot and lost the control of its genetic resources of medicinal plants. Now there is no way out to reject TKDL and had to be accepted. Credit goes to Prof R.A.Mashelkar and his brilliant team members. "Designed as a tool to assist patent examiners of major intellectual property (IP) offices in carrying out prior art searches, the TKDL is a unique repository of India's traditional medical wisdom. It bridges the linguistic gap between traditional knowledge expressed in languages such as Sanskrit, Arabic, Persian, Urdu and Tamil, and those used by patent examiners of major IP offices. All TKDL information is structured along the lines of a patent application. India's TKDL is proving a powerful weapon in the country's fight against erroneous patents and sometimes referred to as biopiracy."[16] TKDL on traditional medicinal plants and its medicinal properties is India's innovative Traditional Knowledge Resource Classification system, in a very structured way and is also modelled on the WIPO International Patent Classification (IPC) and linking

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[15] R P Singh of the IGRI in a conversation with Vandana Shiva, cited in Vandana Shiva, Radha Holla-Bhar, Piracy by Patent: The Case of the Neem Tree. Available at http://www.icta.org/doc/shiva%20holla-bhar.pdf. Visited on 24th April, 2009, at 11 AM.

[16] Prof. V.K.Gupta, Protecting Indian Traditional Knowledge from Biopiracy. Available at http://www.wipo.int/meetings/en/2011/wipo_tkdl_del_11/pdf/tkdl_gupta.pdf. Visited on 4th April, 2011 at 2.40 PM.

with this internationally accepted IPC. It has an integrated global biopiracy watch system that enables monitoring of patent applications around the world related to Indian medicinal systems and effectively detecting of attempts to misappropriate this knowledge, resulting in immediate corrective action to prevent these attempts. TKDL has done something remarkable, effective and practical and problem solving. The then Director General of WIPO is very mush appreciative of the works done by TKDL by saying that "one recent tangible outcome of India's strong involvement was the adopting by IGC technical standards concerning TK documentation"[17] The then Deputy Director general echoed the same view: "TKDL presentation at IGC brought strong recognition for leading work of India in the fields of traditional knowledge."[18]

Traditional Knowledge Digital Library: A tool for prevention of misappropriations of traditional knowledge.[19] The following is the verbatim transcription regarding the aforesaid subject as explained by TKDL itself regarding what TKDL is, what is its function and how does it function.

"TKDL targets Indian Systems of Medicine, viz., Ayurveda, Unani, Siddha and Yoga available in public domain. This is being documented by sifting and collating the information on traditional knowledge from the existing literature existing in local languages such as Sanskrit, Urdu, Arabic, Persian and Tamil in digitized format, which will be available in five international languages which are English, German, Spanish, French and Japanese. Traditional Knowledge Resource Classification (TKRC), an innovative structured classification system for the purpose of systematic arrangement, dissemination and retrieval was evolved for about 5,000 subgroups against few subgroups available in International Patent Classification (IPC), related to medicinal plants. The information is being structured under section, class, subclass, group and subgroup as per the International Patent Classification (IPC) for the convenience of its use by the international patent examiners. Information comprising about 2 lakh formulations has been transcribed for realizing the objective of TKDL Project.

Each Sloka is read and converted into a structured language using Traditional Knowledge Resource Classification by subject (Ayurveda, Unani, Siddha or Yoga) experts. The codes are then filled into the data entry screen. The Slokas are also saved in the database. The translated version of all the TKRC codes is ported in the database. The abstraction is done by the subject experts. The codes once saved in meta data directory are converted in different languages based on Unicode technology. The formulations are presently being converted into English, German, French Japanese and Spanish languages. The converted format of the formulation is readable and can be understood by a layman though it is targeted towards a patent

[17] http://www.tkdl.res.in/tkdl/LangDefault/common/abouttkdl.asp?GL=Eng. Visited .13.2009 at 7 PM.
[18] Ibid.
[19] Available at http://www.tkdl.res.in/tkdl/. Visited on 17th March 2011, at 11 PM.

examiner.

TKDL software with its associated classification system i.e., TKRC converts text in local languages into multiple languages as mentioned above. It may be noted that the software does not transliterate, rather it does a knowledge-based conversion, where data abstracted once is converted into several languages by using Unicode, Metadata methodology. Software also converts traditional terminology into modern terminology, for example, Jwar to fever, Turmeric to Curcuma longa, Mussorika to small pox etc.

TKDL includes a search interface providing full text search and retrieval of traditional knowledge information on IPC and keywords in multiple languages. The search features include single or multiple word searches, complex Boolean expression search, Proximity search, Field search, Phrase search, etc in the form of simple and advance search options. Simple search lets the user search a combination of keywords. Advance search lets the user search using Boolean expressions, using the expressions like "near", "and", "and not". Searches are also available on IPC and TKRC codes.

TKDL acts as a bridge between formulations existing in local languages and a Patent Examiner at a global level, since the database will provide information on modern as well as local names in a language and format understandable to Patent Examiners. It is expected that the issue of the gap on lack of access to prior art traditional knowledge shall get addressed."

TRADITIONAL KNOWLEDGE DIGITAL LIBRARY OUTCOMES AGAINST BIO-PIRACY

After conclusion of the access agreement with the European Patent Office, citation of TKDL references as prior art have led to significant strides towards achieving the goal of preventing misappropriation of Indian Traditional knowledge.[20] In just under two years, in Europe alone, India has succeeded in bringing about the cancellation or withdrawal of 36 applications to patent traditionally known medicinal formulations. The key to this success has been TKDL, a database containing 34, 00,000 pages of formatted information on some 2,260,000 medicinal formulations in multiple languages. Prof. V. K. Gupta has observed that "the impact of the TKDL is already being felt at the EPO. Since July 2009, the EPO's TKDL team has identified 215 patent applications relating to Indian medicinal systems for which third party TKDL evidence has been filed. In two such cases the EPO has already reversed on the strength of TKDL evidence, its earlier intention to grant the patents. In one case the applicant modified the claims submitted and, in 33 other cases, the applicants themselves withdrew their four to five-year-old applications upon presentation of TKDL evidence, a tacit admission of biopiracy by the applicants themselves. It is

[20] Available at http://www.tkdl.res.in/tkdl/langdefault/common/outcome.asp?GL=Eng. Visited on 20th May 2011 at 6.01 PM.

expected that in the coming months some 179 cases that are currently in the balance will either be rejected by the EPO or withdrawn by the applicants themselves. A recent study by a TKDL expert team at the EPO shows a sharp decline (44%) in the number of patent applications filed concerning Indian medicinal systems, particularly in relation to medicinal plants. The TKDL is clearly proving to be an effective deterrent against biopiracy."[21]The following are the examples of such setting aside decisions and withdrawals.

Setting aside of decisions to grant patents or cancellation of intent to grant patent

S.No	Pub.No	Title	Applicant	Date of Filing	Date of TKDL Evidence	Decision to cancel the grant of patent
1	EP1747786	Natural product in cream with anti-vitiligo therapeutic properties	Perdix Eurogroup, S.L., Spain	24-Jul-06	8-Jul-09	27-Jul-09
2.**	EP1520585	Cancer treatment using natural plant products or essential oils or components from some pistacia species	Data Medica Padova, S.P.A., Italy	24-Sep-04	9-Jul-09	14-Jul-09
3.*	EP1849473	Chinese traditional medicine composition	Livzon Pharmaceutical Group Inc., CN, China	19-Jan-07	20-May-10	10-Jun-10

[21] Dr V.K.Gupta, "Protecting Indian Traditional Knowledge from Biopiracy". Available at http://www.wipo.int/meetings/en/2011/wipo_tkdl_del_11/pdf/tkdl_gupta.pdf. Visited on 4th April, 2011, at 2.40 PM.

		for treatment of avian influenza/Bird Flu, method for preparation, and application thereof				

Patents Withdrawn

S.NO	Pub No	Title	Applicant	Date of Filing	Date of TKDL Evidences	Date of Withdrawal	Period between TKDL Evidences and withdrawal of application by applicant (in weeks)
1.	EP1607006	Functional berry composition	UNILEVER NV, Netherland	18-June-2004	17-July-2009	04-Aug-2009	3
2.	EP1781309	Nelumbinis semen extract for preventing and treating ischemic heart disease and pharmaceutical composition and health food containing	Purimed Co. Ltd. Seoul, Korea	09-June-2005	17-July-2009	18-Sept-2009	9

		the same					
3.	EP2044850	Method for altering the metabolism characteristic of food products	Clara's ApS, Denmark	19-Sept-2007	25-Aug-2009	30-Oct-2009	11
4.	EP1889638	Medicaments and food for treatment or prevention of obesity and/or diabetes containing cicer arietinum extract	Jumpsun Bio-Medicine (Shanghai) Co. Ltd, China	06-March-2006	11-June-2009	20-Nov-2009	23
5.	EP1807098	Herbal compositions for treatment of diabetes	Amcod Limited, Mombasa, Kenya	13-Sept-2005	01-July-2009	24-Nov-2009	21
6.	EP1967197	Use of preparations, purifications and extracts of aloe	Cognis IP Management GmbH, Germany	09-March-2007	20-July-2009	27-Nov-2009	19
7.	EP2065031	Skin treatment composition	Evonik Goldschmidt GmbH,Germany	30-Nov-2007	07-Sept-2009	27-Jan-2010	20
8.	EP2090315	Method and system for producing medicinal alcohol as a prophylatic	Kapur MBBS, B., Dr. 9 Hilltop Close Maltby, Rotherham South Yorkshire S66 8QF/Great Britain	13-June-2007	13-oct-2009	18-Feb-2010	18

		or remedy for cancer, HIV, AIDS and autoimmune diseases					
9.	EP1906980	Method of treatment or managment of Stress	Natreon Inc. 2-D Janine Place New Brunswick, NJ 08901/United States	27-July-2006	06-July-2009	25-March-2010	40
10.	EP1660106	Biotherapeutics for Mitigation of health disorders from Terminalia Arjuna	Avesthagen Limited Unit 3, Discoverer, 9th Floor International Tech Park Whitefield Road Bangalore 560 066 / India	15-Aug-2003	08-July-2009	6-April-2010	38
11.	EP1825845	Cosmetic herbal compositions	Jan Marini Skin Research Inc. 6951 Via del Oro San Jose, California 95119/United States	22-Feb-2007	02-July-2009	08-April-2010	37
12.	EP2015761	Methods and composition for treating Sore Throat	Naveh Pharma (1996) Ltd. P.O. Box 8139 42505 Netanya/Israel2009/04	29-March-2007	13-Aug-2009	15-April-2010	35
13.	EP1937231	"Pharmaceutical compositions for the treatment of Chronic Obstructive Pulmonary Disease"	GW Pharma Limited Porton Down Science Park Salisbury, Wiltshire SP4 OJR/Great Britain	11-Oct-2006	21-May-2010	24-June-2010	6
14.	EP2094287	Compositions and methods of	Ocumedic APS Advokat Carlo Siebert	22-Nov-2007	16-June-2010	6-July-2010	4

		using same for treatment of a disease or disorder of the eye and/or the adnexa of the eye	Vimmelskaftet 43 1161 Copenhagen K / DK[2009/36]				
15.	EP1959977	Compositions for regulating intestinal disorders and methods of use thereof	Jaffe, Russell M. 10430 Hunter View Road Vienna VA 22181 / United States[2008/49]	7-Nov-2006	30-June-2010	6-July-2010	1
16.	EP2133089	Compositions for the treatment of disorders of the upper respiratory tract and influenza syndromes	Indena S.p.A. Viale Ortles, 12 20132 Milano / Italy[2009/51]	12-June-2008	07-May-2010	26-July-2010	11
17.	EP2133080	Compounds containing equol	Haelan Schweiz GmbH Schützenstrasse 188808 Pfäffikon Switzerland [2009/51]	13-June-2008	12-July-2010	26-July-2010	3
18.	EP2070545	Oral compositions for the prevention and treatment of inflammatory disorders of the colon	Bios Line S.p.a. Viale Finladia 4 35020 Ponte S. Nicolo (PD) / Italy[2009/25]	10-Dec-2008	14-June-2010	29-July-2010	7
19.	EP2101	Extracts	Aché Laboratórios	14-	01-	30-July-	6

	800	from the skin of fruits of plants from genus vitis, compositio ns containing the same and a process for its manufactur e	Farmacêuticos S.A. Rodovia Presidente Dutra Km 222,2 Porto da Igreja 07034-904 Guarulhos- SP /Brazil [2009/39]	Dec-2007	July-2010	2010	
20.	EP1949 889	Fibroblast activator, method for activation of fibroblast, collagen synthesis promoter, method for promotion of collagen synthesis, skin aging-preventing agent, and method for prevention of aging of the skin	Mercian corporation 5-8, Kyobashi 1-chome Chuo-ku, Tokyo 104-8305 / Japan[2008/31]	17-Oct-2006	07-June-2010	4-Aug-2010	9
21.	EP1709 995	Asthma/alle rgy therapy using nigella sativa	Al-Jassim, Rawaa 2578 River Wood Drive Napperville, Illinois 60565 / United States,Great Britain,Germany,Net herlands and Qatar	02-Marc h-2000	18-June-2009	18-Aug-2010	60
22.	EP1958	Treatment	Bionature E.A.	16-	23-	22-Sept-	64

	641	and prevention of inflammation	Limited 1 Poseidon 2406 Egomi, Nicosia/ Cyprus [2008/34]	Feb-2007	June-2009	2010	
23.	EP2116253	Novel phyllanthus extract	Phytrix JV, LLC 999 18th Street Suite 3210 Denver CO 80202 / United States [2009/46]	07-May-2008	03-Aug-2010	28-Sept-2010	8
24.	EP1729593	Cysteine Protease From Ginger (Zingiber) As A Food Improver And Anti-Inflammatory	Natbio Pty Ltd. 41/8 Goodwin Street Kangaroo Point, QLD 4169 / Australia [2006/50]	23-Feb-2005	30-Oct-2009	11-Oct-2010	49
25.	EP1971354	Composition comprising liquiritigenin for preventing and treating liver disease	Seoul National University Industry Foundation San 4-2, Bongcheon-dong, Gwanak-gu Seoul 151-818 / South Korea [2008/39]	05-Jan-2007	04-May-2010	21-Oct-2010	24
26.	EP2089505	Reduced-hangover alcoholic beverage	Morning-After Herbal Infusion Corporation 180 Boul. rené-Lévesque East Suite 208 Monréal, QC H2X 1N6 / Canada [2009/34]	08-Nov-2007	14-June-2010	29-Oct-2010	19
27.	EP1942917	Compositions and methods for using juice organic,	Juice Beauty 711 Grand Avenue, Suite 290 San Rafael, CA 94901 / US	30-Oct-2006	02-July-2010	04-Nov-2010	18

		juice based skin care products					
28.	EP2175 848	Therapeutic uses of Cannabigerol	GW Pharma Limited Porton Down Science Park Salisbury Wiltshire SP4 0JR / Great Britain [2010/16]	25-June-2008	30-July-2010	11-Nov-2010	15
29.	EP2218 455	Dolichos biflorus extract for use in therapeutic skin treatment	Cognis IP Management GmbH Henkelstrasse 67 40589 Düsseldorf / Germany[2010/33]	07-Feb-2009	30-Sept-2010	18-Nov-2010	7
30.	EP2014 295	Topical compositions for the prevention and treatment of inflammatory and/or infective conditions of the genital area	Velleja Research SRL Via Natta, 28 29010 Pontenure (PC) / Italy [2009/03]	28-May-2008	01-Oct-2010	23-Nov-2010	7
31.	EP2008 661	Formulation based on marigold aloe and centellae	Spannagel, Lucia Antonia Guemes 235, barrio Los Eucaliptos Villa Carlos Paz Provincia de Cordoba / Argentina[2009/01]	05-May-2008	20-May-2010	05-Jan-2011	33
32.	EP1759 706	Use of mash of Gentiana root and corresponding agents	Priebe, Ingrid Thierschstrasse 10 83471 Schönau / Germany[2007/10]	04-Sep-2006	25-June-2010	15-Feb-2011	33
33.	EP2091	Treatment	Biorigin Scandinavia	13-	11-	18-Feb-	36

	353	of Ectoparasitic Infestation	AS Arbinsgate 4 0253 Oslo / Norway[2010/23]	Nov-2007	June-2010	2011	
34.	EP2167072	Use Of Oleocanthal For Treatment Of Cutaneous Inflammation	B.C. DEVELOPMENT S.A. route de France 17 / CP 18 2926 Boncourt / Switzerland,Sprim 2 Square Pétrarque 75016 Paris / France	04-July-2008	21-July-2010	09-March-2011	33
35.	EP1789065	Biologically Active Composition	Bio-Quant, Inc. 6191 Cornerstone Court E., Suite 101 San Diego, CA 92121 / United States	05-Aug-2005	24-Jun-2010	11-Apr-2011	41

CANADIAN INTELLECTUAL PROPERTY OFFICE (CIPO)

S.No	Application.No	Title	Applicant	Date of Filing	Date of TKDL Evidence	Declaration as Dead Application	Period between TKDL Evidence and declaration as Dead Application (in weeks)
1.	CA 2579562	Method for improving sleep behaviors	Johnson & Johnson Consumer Companies Inc, United States of America	26-Feb-2007	24-Sept-2010	28-Feb-2011	22 weeks
2.	CA 2366318	Novel pharmaceutical, dietary and cosmetic compositions	IDA ROYALTY APS, Denmark	02-March-2000	25-Nov-2010	02-Mar-2011	14 weeks

		comprising zinger officinale roscoe, eicosapentaenoic acid and/or docosahexaenoic acid					
3.	CA 2387703	Method for calming human beings using personal care compositions	Johnson & Johnson Consumer Companies Inc, United States of America	29-Feb-2000	10-Sep-2010	11-Feb-2011	22 weeks

CONCLUSION

These two revocation cases, one rejection incident, decisions of non-granting of patents and some withdrawal incidents bring some truths. These are:

A.Two revocations-one turmeric and another neem patent revocation by USPTO and EPO are no doubt great and significant achievement but actually these are nothing. There are hundreds and thousands of traditional knowledge based patents are still operative all over the world-USA. Germany, Japan, Canada etc. The industrial houses-national and multinational corporations are commercialising and earning without paying substantial amount to the knowledge holders. Unless those patents are revoked, profits are returned, exemplary punishments are given, compensations are awarded, the object to have bio-piracy world cannot be achieved. The aim also would remain elusive if existing laws are not amended or new laws enacted to ensure no grant on traditional knowledge.

B. The concern about the vulnerability of traditional knowledge being pirated has taken an ugly turn when patents are granted on researchers and companies in India. Even CSIR has so many traditional knowledge based patents. When India is fighting the traditional knowledge based patents dubbing them as examples of bio-piracy, the incidents of granting of Indian patents of the medicinal properties or processes on herbal and biological resources is definitely to weaken the fight. It would be literarily impossible to convince the international community to accept Indians suggestions to amend the laws or to make laws to fight against bio-piracy. It would be a loss of face to them if they say that "India grants traditional knowledge based patent in their own country but does not want us to grant same kinds of patents". Now it is to be seen and ascertained the nature of these traditional knowledge based Indian patents. Now, the

argument to support this is that any one of those particular patents is not indeed invalid, because novel and non-obvious inventions can build on, or be derived from, publicly available information-traditional knowledge by extensive research. This is possible if the invention though derived from the existing traditional knowledge by taking leads from it, shows intelligible differentia between the existing knowledge or the claimed invention product or process and shows the features of novelty or inventive step. If this is the argument which has merit to a great extent, it needs the reappraisal and revisit of all such suggestions to cover this type of invention by the proposed international and national legislative frameworks. Unless it is ensured that any claim of invention; may be novel or non-obvious in nature and characteristics, derived from traditional knowledge related biological resources in any form and in any manner, is not a subject matter of patent, the object will not be fulfilled. It means that knowledge in any form in public domain can be utilised for academic or research purposes but inventing something and its subsequent commercialisation cannot be allowed. Intellectual property law of all countries does not grant patent on public domain knowledge, it is good. But exploiting the present knowledge to get clues to build upon something, even if novel or non-obvious and commercialisation is allowed. Developed form of PDK can be commercialised which was not possible without the active base of PDK. The reason for which public domain knowledge was excluded from patentability, that very reason is frustrated for this. It means paving the way for exploitation of PDK for personal gain. But if the so called invention is used for the benefit of the society or the entire living or non-living creatures, there should not be any objection. This is the correct approach to protect public domain knowledge. This paradigm shift of approach is must. It is not only for bio-medicine but for all types of intellectual property rights. But this is not applicable to an invention of a perfectly new medicinal value which was not known in oral description or written anywhere.

C. There was no sincere attempt from the Indian government's side for the protection. Government's apathy, indifferent attitude, lack of foresightedness to foresee the imminent danger and to take precautions to successfully overcome those problems and lack of seriousness to take immediate action are some of the causes of this insincerity. Whatever India lost and would be going to lose, it could have been substantially lessened had Government's role been positive, had TKDL been established decades before along with its accomplished works. Moreover, in spite all such biasness and unfairness in the legal frameworks of TRIPs and USA Code on IPR, India could have challenged and got cancelled many bio-pirated patents by the legal use of very limited scopes of 'novelty' and 'non-obviousness' criterion. India failed to utilise those very limited opportunities. Now the question is what those steps are. Firstly, TKDL type of documentation for the known medicinal properties should have been started and completed much earlier even before WTO agreement came into being. Secondly, after getting the leads and clues from the traditional knowledge massive research works should have been started and completed. The results: the medicinal properties of biological resources about these are non-original inventions

should also have been printed and published Thirdly, Prior use of the medicinal plants in every part of India, right from metropolitan cities down to small villages even at the remotest part of the country, should have been properly documented and published.