

# Review on Present Status and Future of Herbal Medicine

Kalyan Kumar Rana<sup>†,a</sup> and Suparna Rana<sup>‡,b</sup>

<sup>a</sup> Department of Chemistry, Gushkara Mahavidyalaya, Gushkara, Burdwan, WB, 713128, India.

<sup>b</sup> Department of Applied Science, Haldia Institute of Technology, Haldia, Purba Medinipur, WB, 721657, India.

Date of Submission: 20<sup>th</sup> May, 2014

Date of Acceptance: 11<sup>th</sup> June, 2014

## Abstract

The number of patients seeking herbal therapy is growing very rapidly. Herbal medicines are now in great demand in the developing world for primary health care not because they are relatively cheap but also for better cultural acceptability, improved matching with the human body and negligible side effects. Though, recent observations indicate that all herbal medicines may not be safe since severe consequences are reported for some herbal remedies. Most herbal products in the market today have not been passed through drug approval processes to demonstrate their safety and efficacy. Thousands of years of traditional use can provide us with valuable guidelines to the selection, preparation and application of herbal formulations. In the present review our endeavor is to describe the present status and the future of herbal medicine.

**Key words:** Herbal medicine, synthetic drug, safety, herb-drug interaction, WHO guidelines.

## 1. Introduction

Plants have been used for health and medical purposes for several thousands of years. It is estimated that about 50,000 species have been used in some cultures for medicinal purposes. A lion part of the global population in developing countries still have faith on

---

<sup>†</sup> Corresponding author, Email: [kalyankrana@yahoo.co.in](mailto:kalyankrana@yahoo.co.in).

<sup>‡</sup> Email: [ranamandal@yahoo.co.in](mailto:ranamandal@yahoo.co.in).

herbal medicines to meet its primary wellbeing needs.<sup>1</sup> This is principally because of the universal belief that herbal drugs are without any side effects besides being cheap and locally available.<sup>2</sup> Making use of botanical products for remedial purposes predates human history and constitutes the origin of modern medicines. Even a century ago, widely used modern drugs were plant based. Examples include aspirin (from willow bark, genus *Salix*), digoxin (from foxglove, *Digitalis purpurea*), quinine (from cinchona bark, *Cinchona calisaya*) and morphine (from the opium poppy, *Papaver somniferum*).<sup>3</sup> It is generally observed that medical history from the beginning is packed with descriptions of individuals who utilized herbs to cure the ill people. However, parallel to the onset of the industrial revolution we witnessed the rise of allopathic or synthetic medicines.

## 2. Why People Use Herbal Medicine

The oldest support of human's use of herbs for healing dates back to the Neanderthal age.<sup>4</sup> Now a days, even with the availability of much modern medicines, there are various reasons for patients turning to herbal therapies. This sort of medications are sometimes cited as a 'sense of control and a mental comfort from taking action,' that helps explain why patients with chronic or incurable diseases *viz.*, diabetes, arthritis, cancer or AIDS are taking herbal medicine. In such situations, they often think that conventional medicine has failed them. In rural areas, there are additional cultural factors which encourage the use of botanicals, such as the environment and culture that is in other words, a 'man earth relationship.' It is a common belief that where an area gives rise to a particular disease, it will also support plants that can be used to cure it.<sup>4</sup> Particularly in India, a densely populated country, large segment of the rural population have almost no access to modern medicine.<sup>5</sup> Hundreds of primary health centers which are intended to serve rural areas, generally lack adequate staffs, basic diagnostic facilities and enough supply of drugs. The rural population is, therefore, compelled to depend greatly on traditional medical systems<sup>6</sup> and in practice, natural plant remedies are accepted to be healthier than synthetic medicine.<sup>7</sup>

## 3. Safety Issues of Herbal Medicines

As herbs are plants, they are often accepted as natural and therefore, safe.<sup>8</sup> In reality, this is not the case is evident from recent reports and reviews<sup>8-10</sup> that include effects of biologically active ingredients of herbs, side effects caused by contaminants and outcome of herb-drug interactions. A particularly miserable case illustrates<sup>11a-c</sup> over 105 patients in Belgium who had been taking a Chinese herbal product from *Aristolochia fangchi* for weight loss and developed Chinese herb nephropathy (CHN, a fatal disease of kidney) caused by the herb. Out of these patients 43 patients developed end-stage renal failure and 39 patients were tested for urothelial carcinoma. Eighteen of these patients were found to have urothelial carcinoma, which was shown to be related to the formation of DNA adducts from the known neurotoxin aristolochic acid found in this herb and another 19 patient showed mild to moderate dysplasia (abnormal development or growth of tissues, organs or cells).<sup>11a-c</sup> A

report of the British Medical Journal (1996)<sup>11d</sup> described that podophyllum poisoning had developed into miniepidemic in Hong Kong. The poisoning was caused by ingestion of the herb known in Cantonese as *Gwai Kou*, which is derived from the roots and rhizomes of *Podophyllum hexandrum*. Another common toxicity to herbal medicines involves complex molecules of pyrrolizidine alkaloids found in certain plants which are either intentionally or unintentionally added to herbal medicines. These alkaloids produce rapidly progressive and fatal hepatotoxic effects.<sup>12</sup>

To be true, it has been reported<sup>13</sup> that herbal products from Asia are particularly problematic since it contains a number of contaminants. A study examining the contents of 260 Asian patent medicines found that 25% of the products contained high levels of heavy metals and 7% contained undeclared drugs, purposefully and illegally added to produce one or more desired effects.<sup>14</sup> Some herbs are known to interact with pharmaceutical or allopathic drugs, though most of these information come from case reports rather than any systematic investigations.<sup>10</sup> For example St John's wort (*Hypericum perforatum*), used to increase a sense of consciousness, inner strength and a number of other effects is the most notoriously interactive herbal product and has been shown to interfere with several drugs metabolized by the cytochrome P-450 liver enzymes, including protease inhibitors, chemotherapeutic drugs, and oral contraceptives.<sup>15</sup> Some authorities note that many herbs, including kava (*Piper methysticum*, native to the Pacific islands, root product used as a sedative), valerian (*Valeriana officinalis*, native to Eurasia, dried rhizomes used as a sedative) and St. John's wort, have the potential to interact with anesthetic agents, amphetamines, amino acids (tryptophan and tyrosine), anti-asthmatic inhalants and other drugs given in the pre- and post-operative period.<sup>16</sup> Presence of highly pharmacologically active substances in herbal medicine is also a cause of headache of the scientists since these offer potential side effects, for example, ephedra, containing the alkaloid ephedrine, famous for its weight loss and energy enhancing abilities, was found to be strong enough to increase the risk of nausea, vomiting, psychiatric symptoms, and palpitations.<sup>17,18</sup> Again, the potential for toxicity from certain herbs is compounded by the frequent use of misleading marketing information. Illegal and erroneous marketing claims for herbal products are common especially in developing nations. A study showed more than half of the herbal products illegally claimed to treat, prevent, diagnose, or cure specific diseases.<sup>19</sup>

In fact most herbal products in the market today have not been subjected to drug approval process to demonstrate their safety and effectiveness. Some of them found to contain mercury, lead, arsenic,<sup>20</sup> corticosteroids and poisonous organic substances<sup>21</sup> in harmful amounts. The majority of *Ayurvedic* formulations available in the market today is spurious, adulterated or misbranded.<sup>22</sup> Most commercially available preparations do not even obey the preliminary rules of the ancient *Ayurvedic* texts. Generally, the herb loses their medicinal properties more or less a year after collection, powders made from them remains effective for around six month and the pastes or ointments for one year. Formulations usually do not carry an expiry date and probable potential side-effects. In absence of a quality control

system, there is no guarantee that the herb contained in the bottle is the same as what is declared on the label. The widespread ignorance and deliberate carelessness towards quality control in the health food industry has stained the name of many important medicinal herbs. It is, therefore, essential to establish internationally recognized and strict guidelines for assessing the quality of herbal medicines. The World Health Assembly (WHA, a forum of WHO) the world's highest health policy setting agency comprised of health ministers from 194 member nations – in its resolutions WHA31.33 (1978), WHA40.33 (1987) and WHA42.43 (1989) has emphasized the need to ensure the quality of medicinal plant product by using modern control techniques and applying suitable international standards.<sup>23</sup>

#### **4. Need for Clinical Trials**

To achieve public faith and to bring herbal product into mainstream of today's health care structure, the researchers, manufacturers and the regulatory authorities must follow rigorous scientific methodologies and comprehensive clinical trials to ensure the quality and lot-to-lot consistency of the herbal products. Correct identification of the desired plant, purification of the intermediates and the final products upto its expected standard of purity and uncompromising consistency of the product quality should be the basis of the production of herbal remedies. A well-organized and legal clinical trial is also the prerequisite of a herbal product to appear in the market. To maintain the quality, effectiveness and safety, on behalf of the producers, there is no other way but to follow the good manufacturing practices and proper preclinical tests.

#### **5. Herbal Medicine--Global Status**

The extensive application of herbal medicine is not limited to developing countries since it has been estimated that almost 70% of the allopathic doctors in France and Germany regularly prescribe herbal medicines.<sup>24</sup> In reality, in these two countries herbal medicines are sold as prescription drugs and are covered by national health insurance schemes. The number of patients in search of herbal products for their healing is also rising very rapidly.<sup>25</sup> As the US Food and Drug Administration (FDA) relaxing guidelines for the sale of herbal supplements<sup>26</sup> the market is thriving with herbal products.<sup>27</sup> It was estimated that the herbal medicine market<sup>1</sup> in 1991 in the countries of the European Union was about \$6 bn (may be over \$30 bn now), with Germany account for \$3 bn, France \$1.6 bn and Italy \$0.6 bn. In 1996, the US herbal medicine market<sup>1</sup> was about \$4 bn, which have tripled by now. The Indian herbal drug market is about \$1 bn and the export of herbal crude extract is about \$80 mn.<sup>1</sup> In the last few decades, a curious thing has been observed to botanical medicine. Instead of being ruined by allopathic medicine and related pharmaceutical industry, it has made a successful come back. Herbal medicine has benefitted from the purposeful investigation of the medical science, while whimsical and emotional claims for herbal cures have been thrown away, acknowledging herbal treatments and plant medicine that actually works. Developed practically by trial and error, many herbal treatments were yet remarkably

effective.<sup>28</sup> A study<sup>29</sup> estimated that 39% of all 520 new approved drugs in 1983-1994 were natural products or easily derived from natural products and 60-80% of antibacterial and anticancer drugs were derived from natural products.<sup>30</sup> Penicillin which replaced mercury in the treatment of syphilis and put an end to so many lethal epidemics comes from plant mold. Belladonna (*Atropa belladonna*) still provides the chemical used in ophthalmological formulations and in antiseptics used to treat gastrointestinal disorders. Indian snake root or *Sarpagandha* (*Rauwolfia* or *Rauwolfia serpentina*) containing the bioactive ingredient, reserpine, was the basic constituent of a variety of tranquilizer first used by RW Wilkins in the 1950's to treat certain types of emotional and mental problems. Though reserpine is seldom used today for this purpose, its discovery was a breakthrough in the treatment of mental illness. Inspection of the history of medicine exposes a definite pattern. Humankind first utilized resources found in the nature on an experimental basis to cure various ailments.<sup>31</sup> The plant, animal parts and even microorganisms were primarily employed in unchanged form and afterward concentrated extracts to improve their activity. Subsequently, pure synthetic chemicals possessing even greater activity were developed as modern medicine.<sup>32</sup>

In fact, plant substances play an important role even today especially for treating heart diseases, hypertension, mental illness, pain, some form of cancer, asthma, neurological disorders, dyspepsia, liver diseases and other ailments.<sup>25, 33-36</sup> Several prescription drugs sold in United States are molecules derived from or modeled after naturally occurring molecules in plant. Interest in plant product research has been reawakened by discoveries of anti-cancer and memory enhancing activity of bioactive molecule bryostatin from marine species of bryozoans (*Bugula neritina*) and potent new chemotherapeutic agent taxol from the plant *Taxus brevifolia*. However, in spite of increase in enthusiasm for herbal medicine, an increasing number of aged traditional healers are dying with their enormous knowledge and experience left unrecorded. At the same time, forests, too often disappear without any notice to the learned community. Almost 12.5% of all plant species are threatened with immediate extinction. This estimate by the International Union for the Conservation of Nature (IUCN, headquarters in Gland, Switzerland, near Geneva) is respected by most botanists as authentic, since it considers only the species known to science while numerous undiscovered species wipeout from the world unrecorded and unspoken.<sup>37</sup>

## 6. Herbal Medicine--Indian Status

India has a wealthy ritual of herbal medicine as evident from *Ayurveda*, which could not have flourished for two thousands of years without any scientific base. *Ayurveda* which literally means knowledge (*Veda*) of life (*Ayur*) had its beginning in *Atharvaveda* (Circa 1500-1000 BC). *Charak Samhita* and *Shushruta Samhita* are the two most famous treatises of *Ayurveda*. Several other texts were written over the centuries such as *Bela Samhita*, *Kashyap Samhita*, *Agnivesh Tantra*, *Vagabhata's Ashtanga hridaya* (600AD) and *Madhava Nidan*

(700AD).<sup>38</sup> Plant products dominated Indian *materia medica* which made extensive use of bark, leaves, flower, fruit, root, tubers, juices etc. The theory of *rasa*, *vipaka*, *virya* and *prabhava* formed the basis of *Ayurveda* pharmacology, which made no clear distinction between diet and drug, nutrition and energy as all were vital components for treatment of illness.<sup>39</sup> *Charaka*, *Shushruta* and *Vagabhata* described numerous herbal drugs with their properties and clinical effects.

On the basis of medicinal properties, in Indian traditional practices, herbal medicines have been classified as appetizer, digestive stimulant, laxative, antidiarrheal, antihaemorrhoid, antiemetic, antipyretic, anti-inflammatory, antipruritic, antiasthmatic, antiepileptic, antihelminthic, haemopoietic, haemostatic, analgesic, sedative, promoter of life, promoter of strength, complexion, voice, semen and sperm, breast milk secretory, fracture and wound healing, destroyer of kidney stones etc.<sup>38</sup> The introduction of western medicine in the eighteenth century was a hindrance to the practice of *Ayurveda*, which suffered considerable neglect at the hands of the colonial administration. After the first success of discovery of reserpine from cinchona or *Sarpagandha* an enormous amount of characterization of medicinal plants was done in many research institutes and university departments, but the outcome was discouraging as the attempts were disordered, limited and nonspecific.<sup>39</sup> Molecular pharmacology now offers a new interface between *Ayurveda* and modern medicine. Using concepts of modern science and technology, diverse categories of *Ayurvedic* drugs could provide novel molecular probes.

## 7. Herbal Medicine and the Market

The average size of the global herbal market<sup>40</sup> is of the order of around \$62 bn dollars per annum. European union nations are the largest market with the share 43% of total herbal market whereas ASEAN countries 19%, Japan 16%, North America 11%, rest of European Union 4% and other countries 7%. Countries like Japan and China have successfully marketed their traditional medicines abroad (recall health tourism). Their alternative therapies are well-accepted in Europe and US. It is expected that the global market for herbal products will be raised up to \$5 Tn by 2050 and subsequently herbal remedies would become increasingly important especially in developing countries. The Indian herbal drug market is about \$1 bn and the export of herbal crude extract is about \$80 mn per annum.<sup>1</sup> India being one of the 12 most biologically diversified countries possess tremendous market potential and remarkable business advantages in this emerging field of trade. Presently, when compared to the Chinese and the Japanese level of penetration in the global marketplace India is not at all figuring anywhere. But there are some positive indications also for us in the global business scenario since India has 16 agro-climatic zones, 10 vegetative zones, 15 biotic provinces, 426 biomes, 45000 different plant species and 15000 medicinal plants that include 7000 *Ayurveda*, 700 *Unani*, 600 *Siddha* and 30 allopathic medicines.<sup>1</sup>

## 8. Future Directions

Several experts have suggested a number of important changes to the regulation of herbs that could improve the safety level and appropriate use of these products.<sup>41,42</sup> The main recommendations are: 1) manufacturers are required to register, as per rule, with the government, 2) safety tests similar to those required for allopathic drugs are mandatory, 3) all health claims to be supported by data approved by the government and 4) product labels must provide an accurate list of all ingredients used. Although these preliminary changes will certainly increase the safety of herbal products, additional changes are also needed to improve and promote high-quality research. If supported and coordinated by one or more appropriately funded institution of the government, the effort to upgrade the standard of the herbal products will be successful. Extensive research with state-of-the-art laboratories, wealthy libraries, publications and encouraging job opportunities are the basic requirement for the competitive future of the herbal remedies. Obviously, there must have some form of patent protection in favor of the manufacturers who invest in expensive studies and documentations, so that the efficacy of their products could be rewarded financially.

## 9. Conclusions

The growth of the pharmaceutical industry and the perpetual development of new and more effective synthetic drugs have not diminished the importance and relevance of medicinal plant products in many societies. Population escalation in the developing world along with increasing awareness in the developed nations has greatly expanded the demand for plant products. The WHO guidelines in supporting the preparation of model code of conduct and strict regulations in western countries for the assessment of the quality, safety and efficacy of herbs have been helpful in strengthening their role in health care industry. The increasing cost of energy and chemical raw materials, serious environmental issues linked with the synthetic drugs, will certainly make herbal remedies even more compatible in near future. If truth be told, peoples have started realizing that many of the modern clinical drugs used for the cure of diseases are dull, evil, burdensome and evidently costly. What is required is the one that is rather secured, efficient and less expensive. Therefore, the role of herbal medicine in providing effective health care services in most rural parts of the world is likely to continue far beyond the 21<sup>st</sup> century.

## References:

1. V.P. Kamboj, *Current Science*, **78**, 35, (2000).
2. L.M. Gupta and R. Raina, *Current Science*, **75**, 897 (1998).
3. A. Vickers and C. Zollman, *B.M.J.*, **319**, 1050 (1999).
4. L.C. Winslow and D.J. Kroll, *Arch. Intern. Med.*, **158**, 2192 (1998).
5. G. Mudur, *B.M.J.*, **314**, 1573 (1997).
6. G. Mudur, *B.M.J.*, **311**, 1186 (1995).
7. W.M. Gesler, *Soc. Sci. Med.*, **34**, 735 (1992).

8. E. Ernst, *Am. J. Med.*, **104**, 170 (1998).
9. S. Bent, R.J. Ko, *Am. J. Med.* **116**, 478 (2004).
10. P.A. De Smet, *N. Engl. J. Med.* **347**, 2046 (2002).
11. (a) J.L. Nortier *et al.*, *N. Engl. J. Med.*, **342**, 1686 (2000). (b) F. Reginster *et al.* *Nephrol, Dial Transplants*, **12**, 81 (1997). (c) J.P. Cosynes *et al.*, *Am J Kidney Dis.*, **33**, 1011 (1999). (d) P.P. But *et al.*, *B.M.J.*, **313**, 117 (1996).
12. F. Stickel, E. Patsenker, D. Schuppan, *J Hepatol*, **43**, 901 (2005).
13. S. Bent, *J. Gen. Intern. Med.*, **23**, 854 (2008).
14. R.J. Ko, *N Engl J Med.* **339**, 847 (1998).
15. P. Hammerness *et al.*, *Psychosomatics*, **44**, 271 (2003).
16. M.K. Ang-Lee and J. Moss, C.S. Yuan, *J.A.M.A.*, **286**, 208 (2001).
17. S. Bent, T.N. Tiedt, M.C. Odden, M.G. Shlipak, *Ann Intern Med.* **138**, 468 (2003).
18. P.G. Shekelle *et al.*, *J.A.M.A.*, **289**, 1537 (2003).
19. C.A. Morris and J. Avorn, *J.A.M.A.*, **290**, 1505 (2003).
20. J. Kew *et al.*, *B.M.J.*, **306**, 506 (1993).
21. P.A.G.M. De Smet, *Adverse Drug Reactions Bulletin*, **183**, 695 (1997).
22. S. Kumar, *The Lancet*, **351**, 1190 (1998).
23. <http://m.biotecharticles.com/Agriculture-Article/WHO-Guidelines-For-Herbal-Drugs-Part-2-912.html>.
24. M.T. Murray and J.E. Pizzorno Jr, Botanical medicine - amodern perspective. In Text Book of Natural Medicine Vol-1 (eds. J.E. Pizzorno Jr, M.T. Murray) Churchill Livingstone, 267-79, (2000).
25. L. Alschuler, S.A. Benjamin and J.A. Duke *Patient Care*, **31**, 48 (1997).
26. S. Gottlieb, *B.M.J.*, **320**, 1623A, (2000).
27. P. Brevoort, *Herbal Gram*, **44**, 33 (1998).
28. J. Dwyer and D. Rattray Anonymous, *Reader's Digest General Book*, 48 (1993).
29. G.M. Cragg, D.J. Newmann, K.M. Snader, *J Nat Prod*, **60**, 52 (1997).
30. A.L. Harvey, *Trends Pharmacol Sci.*, **20**, 196 (1999).
31. S. K. Pal and Y. Shukla, *Asian Pacific Journal of Cancer Prevention*, **4**, 281 (2003).
32. J.E. Robbers, M. Speedie, V.E. Tyler, *Williams and Wilkins*, Baltimore, 1 (1996).
33. A. Vickers and C. Zollman, *B.M.J.*, **319**, 1050 (1999).
34. A.J. Carter, *B.M.J.*, **319**, 1623 (1999).
35. A. Bensoussan *et al.*, *J.A.M.A.*, **280**, 1585 (1998).
36. D. Schuppan *et al.*, *Hepatology*, **30**, 1099 (1999).
37. P.A. Cox, *Science*, **287**, 44 (2000).
38. R.D. Lele, *J Assoc Physicians India*, **47**, 625 (1999).
39. M.S. Valiathan, *Curr Science*, **75**, 1122 (1998).
40. [http://www.dsir.gov.in/reports/ittp\\_tedo/ism/ISM\\_AS\\_Market.pdf](http://www.dsir.gov.in/reports/ittp_tedo/ism/ISM_AS_Market.pdf).
41. J.D. Lewis and B.L. Strom, *Ann Intern Med*, **136**, 616 (2002).
42. D.M. Marcus and A.P. Grollman, *N Engl J Med*, **347**, 2073 (2002).