

Exploring Medicinal Plants: A Gateway to Modern Drug Discovery Innovations

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ABSTRACT

Present medicinal plant drug discovery research utilizes a comprehensive approach that combines herbaceous, plant chemical substances, biochemical, and molecular methods. Throughout history, humans have relied on nature to meet their essential requirements, containing medications to treat an extensive range of ailments. Plants also served as the foundation for complex traditional medicine schemes. Many currently recognized lead compounds for therapeutic agents are natural products or their derivatives. Ethnomedicinal research is critical in developing new medicines derived from native therapeutic plants. Green pharmaceuticals are gaining

prominence with significance due to the unrivaled accessibility of element variety and ordinary inventions, also as pure composites or as homogeneous plant fractions, offer vast opportunities for new drug discoveries. As a result, the requirement for herbal medications and other ordinary inventions derived from a range of plant varieties has steadily increased in recent years. This article examines some of the natural product approaches past successes as well as the challenges in medicine development from ordinary creations, particularly superior plants. The history, current, and potential importance of using knowledge from plants utilized in conventional medicinal practice for the innovation of novel bioactive composites are discussed in this study.

Keywords: Drug discovery, Ethno medicinal, inventions, implementing, innovation

Introduction

Since the dawn of time, therapeutic plants have been utilized as a resource of medication in every tradition [1]. The community initially utilized plants to satisfy their dietary needs. Normal flora reappears as a beneficial resource for fitness enhancement and the healing of numerous ailments across different individual cultures. Several plant varieties are located in several divisions of the globe for remedies against various diseases, such as in Asia, South America, and Africa [2,3,4]. Although the World Health Organization estimated that conventional medicines constitute the principal fitness care method for 60% of the globe's inhabitants, a huge figure of plant varieties through probable organic actions remains unknown [5]. Modern drugs' efficacy is now presumed due to their greater compatibility with the individual body, traditional suitability around the globe, and fewer side-effects [6]. Furthermore, 35,000 plant varieties are utilized for medicinal purposes in different human societies around the world, and approximately 80% of the globe's inhabitants depend on conventional medications, which require the utilization of plant fractions for the majority of the moment [7, 8].

Ethnomedicinal learning is critical for discovering novel medicines from native therapeutic plants and green pharmaceuticals are gaining reputation and significance [9] since the unrivaled accessibility of chemical variety and ordinary inventions, either as pure composites or as homogenous plant fractions, offers vast opportunities for new drug discoveries. Synthetic medicines were endorsed as safe

and effective ten years ago until it was revealed and relabelled due to unexpected side effects [10] [<https://link.springer.com/article/10.1007/s40264-022-01160-9>].

Herbal drugs, alternatively, have no such side effects, and as a result of the combination of therapeutic ingredients with granites and vitamins, they have advantages over conventional medicines [11, 12]. Scientists' attention focused due to ethnomedicines resurgence of expertise in global traditional health practices [13]. As a result, the need for herbal medications and other ordinary inventions derived from a range of plant varieties has steadily increased in recent years. Since the history of ethnobotany, the quantity of modern drugs has been determined, with particular importance on the certification of conventional medicinal plant awareness. Natural or natural product-derived molecules account for 78% of new chemical constituents in medicinal plants, which are being utilized as a potential substitute therapy for communicable ailments [14]. Around 25% of drugs a significant figure of synthetic analogs based on proto-kind-composites obtained from plants, which comprise modern pharmacopoeias [15].

Plants are extremely important in the field of medicine because they have been utilized for thousands of years to treat a broad array of ailments [16]. Since the early 19th century, when morphine was extracted from opium, vigorous composites have been separated from therapeutic plants [17]. As the function of therapeutic plants in drug development was determined, a range of remedies, for instance, quinine, digitoxin, codeine, cocaine, and morphine, were isolated. Several of these medications are silent in utilization nowadays [18]. Numerous therapeutic plant fractions are highly helpful in opposition to infections of microbes and parasites [19]. Antifungal proteins such as chitinase, glucanase, and proteins with small molecular mass and non-enzymatic character, for example, are found in the kernels of several therapeutic plants. These proteins are used to protect a developing embryo from several infections [20].

Botanical medicine, also known as herbal medication, is the utilization of plant kernels, leaves, roots, blossoms, berries, or grows for medicinal purposes. Furthermore, it has been utilized by people all over the world since prehistoric times to cure, control, and handle many diseases [21,22]. Communicable ailments have now happened to a principal reason for death worldwide, making their research a

worldwide apprehension [23]. Multidrug resistance in pathogens is posing a challenge to the therapeutic effectiveness of many currently available antibiotics [24].

Throughout history, herbal medications have been used to cure various communicable diseases. Plant fractions, whether as standardized ordinary inventions or as pure composites, have provided limitless opportunities for new drugs due to their unrivaled chemical diversity. For re-emerging and new infectious diseases, there is an immediate and ongoing need for new antimicrobial compounds with novel mechanisms of action and complex chemical structures [25]. As a result, a growing number of researchers are turning their attention to traditional medicines and attempting to create better antimicrobial drugs [26]. The value of medicinal plants has grown as the breakdown of antibiotic confrontation and chemotherapeutics by pathogenic microbial transmittable mediators has increased, and they have been screened for their possible antimicrobial activity [27].

Through the 19th century, scientists started separating, sanitizing, and recognizing vigorous constituents from therapeutic plant fractions, which led to the detection of several of the majority of significant medicines from therapeutic plants that are now extensively utilized in current medication. Since galegine, a guanidine-nature alkaloid present in *G. officinalis* has blood sugar-decreasing activities. Since the created alkaloid was extremely lethal, various structural analogues of this alkaloid were developed and clinically tested [28][<https://doi.org/10.2174/0929867328666210628131409>] Metformin, an important antidiabetic medication, was developed and marketed as a result of these efforts [29].

Aside from the organically vigorous ordinary inventions obtained from therapeutic plants point out, many ordinary creations gained from therapeutic plants have also been used as "lead composites" in the plan, synthesis, and production of new medicine composites. In a sense, certain natural products extracted from plants have been a little changed to make them extra efficient or less lethal to prepare "semi-synthetic drugs." Aspirin was invented in 1953 as an instance of such a method using the structural alteration of salicylic acid that was discovered as an avigorous constituent in many therapeutic plants with ache-reducing properties

[30].

In current years, there has been a surge of attention in the field of natural product drug discovery research [31] (<https://www.mdpi.com/1420-3049/27/2/349>). Unmet curative requires an extraordinary range of together chemical composition and biological actions of obviously happening secondary metabolites, the efficacy of new bioactive ordinary inventions as biochemical probes, the improvement of new and perceptive practices to identify biologically energetic natural inventions, and progressed tetrahedron. The pharmaceutical industry is focusing its R&D efforts on developing new innovative/indigenous plant-based medicines by pursuing leads from the conventional medical system [32]. Modern medicine is also valued by the World Health Organization, which has established policies and instructions, and criteria for botanical medications. The production and processing of medicinal plants, as well as the manufacture of herbal medicines, involve the application of established agro-industrial technologies [33]. Over the last decade, there has been a revival of attention on natural substances as a resource of possible medical substances. This analysis is not proposed to be a comprehensive examination of natural invention-obtained pharmaceuticals; relatively, it aims to highlight the critical task that natural inventions have participated and carry on to play in the medicine development process as well as its expectations prospects.

Separation and decontamination of vigorous composites from therapeutic plants and further ordinary resources, synthetic chemistry, combinatorial chemistry, and bioinformatics methods (e.g. molecular modeling) have all been utilized to acquire composites for drug innovation [34]. Although pharmaceutical corporations and financial support organizations are becoming more noticed in molecular modeling, combinatorial chemistry, and further synthetic chemistry practices, natural inventions, especially therapeutic plants, continue to be a significant foundation of novel medicines and novel chemical entities, and innovative medicine leads. Before the nineteenth century, plant medications were often utilized in their raw forms, such as decoctions (boiled fractions of growl and root), infusions (herbal teas), syrups, and tinctures (alcoholic fractions) [35].

Externally plants have been used in the form of ointments, poultices and balms, essential oils, and herbal baths. Investigators working on medicinal plants in

developing countries also go through a rigorous training program to be taught the names, uses, and preparations of local plants, and therapeutic plants are advertised together with vegetables and further products in a variety of village marketplaces [36]. The World Health Organization (WHO) has acknowledged that the program for helpful health in developing countries cannot at all be met solely by western medication and that it must be supplemented by other medications, including conventional herbal medications from these states [37]. It has more advised and recommended people use their therapeutic plants and further conventional medication schemes to achieve their main healthcare goals. Patients with chronic diseases in developing countries are reportedly turning to herbal therapies as alternatives to current synthetic medications [38].

According to Shoemaker et al., there are over 400,000 plant species on the planet with a vast pool of bioactive compounds; however, simply a small proportion of these have been studied in research investigations [39]. While bioactive composites from conventional therapeutic plants were tested using screening programs, it was discovered that they had a wide range of healing actions. Consequently, a variety of medicines against tumors and mediators against fungal infections extracted from plants are now available for clinical use. Plants are also an effective as well as consistent resource of agents against tumors, according to another study [40, 41, and 42]. In the last fifteen years, fungal infections have developed confrontation to currently used antifungal medicines as well as the anti-side infectious effects or toxicity. As a result of this, medicinal plants have gained in value due to their antimicrobial and antifungal properties [43].

In developing new antimicrobial drugs, substances with low poisonous to host cells and the ability to hinder pathogens are prioritized. Antimicrobial actions of South Asian therapeutic plants are increasingly being identified [44, 45]. Heinrich and Teoch [46] treated with these plants in local herbal medicine systems a variety of ailments, including infectious diseases. For example, *Terminalia arjuna* bark has been utilized for a range of functions, and the growlis effective in cardiovascular therapy [47]. In the same way, *Andrographis lineate* has been used to treat snake bites [48].

Natural invention chemists arrange fractions from plant substances, screen them in

pharmacologically suitable analysis, and then initiate the method of isolating as well as characterizing the vigorous composites through bioassay-directed fractionation. During the development, along with the execution of effective screening analysis directed at physiologically important molecular intentions, molecular ecology has become critical to therapeutic plant medicine innovation. Pharmacognosy is an interdisciplinary science that combines both of these areas. While the term was initially used about two hundred years ago, the meaning and practice of pharmacognosy has evolved as remedy usage. Then therapeutic plants advanced from the production of rough medicines to the separation of vigorous composites in drug innovation [49, 50, 51]. During together 2001 and 2002, natural inventions or products obtained from natural creations accounted for roughly a fifth of the top-selling medications worldwide [52].

In addition, four novel therapeutic plant-derivative remedies have recently been approved in the United States. Artemisinin, a sesquiterpene lactone derived from *Artemisia annua* L, a plant utilized in conventional Chinese medication, is the source of arteether, a potent antimalarial medication. In Europe, other artemisinin compounds are in different phases of development or medical trials as antimalarial medicines [53, 54]. Galantamine is a natural product that was initially separated from *Galanthus woronowii* Losinskin Russia in the early 1950s thanks to an ethnobotanical lead. Galantamine has been approved and designed for the treatment of Alzheimer's disease, and it works by inhibiting acetylcholinesterase (AChE) with the requisite to modulating the nicotinic acetylcholine receptor (nACh R) [55, 56].

Nitisinone is a recent therapeutic plant-derived medication that treats tyrosinaemia, a rare inherited condition, indicating the utility of natural creations as lead compositions [57]. Nitisinone is a derivative of mesotrione, a herbicide derived from the natural invention *Leptospermum*, which is also found in the *Callistemon citrinus*, Stapf plant (*Melaleuca citrinus*). Myrtaceae is a genus of plants. In both humans and maize, all three triketones inhibit the similar enzyme, 4-hydroxyphenylpyruvate dehydrogenase. Inhibition of the HPPD enzyme functions as a herbicide in maize, reducing plastoquinone and tocopherol biosynthesis, whereas, in individuals, inhibition of the HPPD enzyme avoids tyrosine catabolism and more toxic bioproduct gathering in the liver and kidneys [58, 59]. Tiotropium was

recently endorsed for managing chronic obstructive pulmonary disease in the United States [60, 61]. Tiotropium is an anticholinergic bronchodilator that is inhaled and based on ipratropium, an atropine derivative separated from *Atropa belladonna* Linn. further Solanaceae family plants [62,63]. Compared to other COPD drugs, tiotropium has shown higher effectiveness and longer-lasting effects [64].

Plant-derived drug innovation must be initiated through a combinatorial approach when evaluating candidate compounds. With the emergence of new tools such as profiling procedures, computational biology methods, quantum computing, large statistics, microfluidics, and synthetic smartness, scientists will exploit the medicinal activities of plant derivatives with researching their molecular outcomes in physiological situations [65, 66].

The instruments still lack enough sensitivity to detect in extracts every phytochemical activity [67] [Hosni, S., Gani, S. S. A., Orsat, V., Hassan, M., & Abdullah, S. (2023). Ultrasound-Assisted Extraction of Antioxidants from *Melastoma malabathricum* Linn.: Modeling and Optimization Using Box–Behnken Design. Eliminating potential hindering elements such as polyphenolic tannins has been recommended as one approach to boost screening and make simpler extracts [68]. Pre-fractionation and extraction methods are two recorded groundbreaking techniques that can be used to achieve this [69, 70]. These fraction methods have also affected more punch leads through drug production [71, 72, 73, and 74]. To haul out natural composites competently from plants, inventive tools such as supercritical liquid extraction, semi-bionic extraction, ultrasonic-aided, microwave-aided, molecular distillation process, enzyme-supported extraction, and membrane separation tools can be utilized. These extraction techniques are equivalent to conventional methods in terms of extracting the most composites from the natural invention [75-83, 84, 85, 86, 87]. Currently, many structural analogues of these composites are employed in health centers and hospitals. A variety of novel plant-derived composites is showing promise as drugs against cancers. One of our studies examined the antitumor properties of fractions from African lettuce, a plant widely grown in Africa, mainly in West Africa [89].

Herbal remedy against asthma prepared from fractions of *Glycyrrhiza uralensis*, *Ganoderma lucidum*, and *Sophora flavescens*, for example, relieves

bronchoconstriction in an animal representation while returning cytokine stability, resulting in longer-duration relief against asthma [09]. Only the synergistic action of chemical constituents of the three herbal elements produces the therapeutic effect [91, 92].

Plant-based drugs have become more commonly used as a result of the introduction of Good Industry Practice, and several are nowadays going through scientific trials for FDA approval [93]. Catechin, along with resveratrol, has synergistic effects, according to Skroza and colleagues, as demonstrated by various antioxidant assays [94].

The ferric decreasing capacity of plasma antioxidant analysis was used in similar study to demonstrate caffeic acid and resveratrol synergistic outcomes. A further study demonstrated the synergistic outcomes of ethnomedicinal plants of the Apocynaceae family and antibiotics in opposition to the clinical separation of *Acinetobacter baumannii* [95]. Numerous further studies found that various plant fractions and traditional medicines, such as doxorubicin, have a synergistic effect [96].

Vinca rosea (or *Catharanthus*) alkaloids, taxanes, camptothecins, and epipodophyllotoxins are the four major groups of anticancer compounds commonly approached in clinical trials. *Catharanthus roseus* (L.) G. was used to isolate vinblastine and vincristine. For over 40 years, Don (Apocynaceae) (previously *Vinca rosea* L.) has been utilized in clinical trials [97]. Through binding directly to tubulin and causing its depolymerization, the vinca alkaloids and some of their semi-synthetic imitatives obstruct mitosis through metaphase capture [98]. Despite advances in medicinal plant drug research, prospective endeavors challenge many obstacles. Continuation of other drug discovery projects, phytochemists, pharmacognosists, and other natural invention researchers would require continuously increasing the quality and quantity of composites that reach the medicine production stage. The drug discovery process is expected to acquire a standard of ten years and charge above eight hundred million dollars [99, 100]. The multiple leads rejected through the medicine development procedure consume significant time and resources. Only one out of every 5000 lead compounds is expected to make it during experimental trials and be accepted for utilization. The

primary phase in a prolonged drug manufacturing procedure is lead detection. Lead optimization, lead formulation (including pharmacokinetics, pharmacology, toxicology, ADME [absorption, distribution, metabolism, and excretion], remedy liberation), and experimental trials acquire a long moment.

Since drug innovation from therapeutic plants has historically been slow, and faster with superior plant selection, bioassay screening, composite segregation, and composite production methodologies are needed [101, 102]. Innovative plant collection strategies are required, particularly in light of the official and opinionated matters adjacent to profit distribution agreements [103,104].

Designing, determining, and implementing effective, clinically applicable, elevated throughput bioassays is challenging for all drug development programs [105,106]. Although the purpose of high-throughput screening analysis can be difficult, composite and fraction libraries can be checked for biological action on one occasion a screening analysis is in a position [107]. Screening fraction libraries can be challenging, but modern methods, such as the pre-fractionation of extracts can help solve several of these difficulties. Bioassay screening challenges will increase significance concern in medicinal plant drug innovation expectations. The introduction of new technology is needed to improve the speed of active compound isolation. While nuclear magnetic resonance and mass spectrometry are commonly utilized for composite recognition, a novel process for utilizing NMR and MS to promote compound isolation may be useful for therapeutic plant drug innovation. In addition, high-throughput X-ray crystallography may be used to find new therapeutic plant leads.

Conclusion

Conventional medication is a vague word utilized to describe every non-Western medicinal practice, whereas ethnomedicine can be interpreted generally as the utilization of plants by individuals as remedies. Ethnopharmacology is a broad drug exploration approach involving observing, describing, and testing indigenous drugs and their biological activities. Biochemistry, pharmacology, botany, chemistry, and a variety of further fields all lead to the innovation of biologically active natural inventions. Nature is the 'optimal combinatorial chemist', as shown by the preceding discussion, and natural inventions composites determined from therapeutic plants

have revealed several clinically helpful medicines. Despite the many obstacles faced in developing therapeutic plant-derived drugs, natural inventions separated from plants will continue to be important in the quest for novel medications. By combining current drug discovery methods with the combined efforts of different disciplines, proper use of these sources and techniques in bio panorama would undoubtedly aid in discovering new lead molecules from plants. Continuous advances in the pace of dereplication, separation, structure explanation, and composite provide methods, as well as the careful collection of medicine intentions for the screening of natural product libraries, are key factors in remaining competitive with the modern system of medicine.

References

1. Malik, F., D. Hussain, A.S. Dil, A.Hannan, A.H. Gilani. 2005. Islamic republic of Pakistan. In: Ong, C.K., G. Bodeker, C. Grundy, G. Burford and K. Shein.(Eds.). WHO Global Atlas of Traditional, Complementary and Alternative Medicine (Map Volume). World Health Organization. Geneva. pp. 165–169 (Chapter22).
2. Duraipandiyan, V., M. Ayyanar and S. Ignacimuthu. 2006. Antimicrobial activity of some ethnomedicinal plants used by Palyar tribe from Tamil Nadu, India. BMC Complement. Altern. Med. 6: 35–41.
3. Bolzani, V. da S., M. Valli, M. Pivatto, C. Viegas. 2012. Natural products from Brazilian biodiversity as a source of new models for medicinal chemistry. Pure Appl. Chem. 84: 1837-1846.
4. Khalid, H., W.E. Abdalla, H. Abdelgadir, T. Opatz, T. Efferth. 2012. Gems from traditional north-African medicine: medicinal and aromatic plants from Sudan. Nat. Prod. Bioprospect. 2: 92–103.
5. Li, J.W.H. and J.C. Vederas. 2009. Drug discovery and natural products: end of an era or an endless frontier? Science. 325: 161–165.
6. Verma, S. and S. P. Singh. 2008. Current and future status of herbal medicines. Vet. World. 1(11): 347-350.
7. Lewington, A. 1993. A review of the importation of medicinal plants and plant extracts into Europe. Cambridge, UK; TRAFFIC International. 37 pp.
8. Sandhya, B., S. Thomas, W. Isabel, R. Shenbagarathai. 2006. Ethnomedicinal plants used by the Valaiyan community of Piranmalai Hills (Reserved Forest),

- Tamil Nadu, India. A pilot study. *Afr. J. Traditional Complementary Altern. Med.* 3(1): 101-114.
9. Yaseen, G., M. Ahmad, S. Sultana, A. S. Alharrasi, J. Hussain, M. Zafar and S. Ur-Rehman. 2015. Ethnobotany of medicinal plants in the Thar desert (Sindh) of Pakistan. *Journal of Ethnopharmacology.* 163: 43–59.
 10. Jigna, P. and C.V. Sumitra. 2007. In vitro antimicrobial activity and phytochemical analysis of some Indian Medicinal plants. *Turk. J. Biol.* 31:53-58.
 11. Hussain, F. 2007. Traditional resource evaluation of some plants of Mastuj, District Chitral, Pakistan. *Pak. J. Bot.* 39(2): 339-354.
 12. Lokhande, P.D., K.R. Gawai, K.M. Kodam, B.S. Kuchekar, A.R. Chabukswar and S.C. Jagdale. 2007. Antibacterial activity of isolated constituents and extracts of roots of *Inula racemosa*. *Res. J. Medicinal Plant.* 1: 7-12.
 13. Mahmood, A., S. Rashid and R.N. Malik. 2013a. Determination of toxic heavy metals in indigenous medicinal plants used in Rawalpindi and Islamabad cities, Pakistan. *J. Ethnopharmacol.* 148: 158–164.
 14. Samuelsson, G., 2004. *Drugs of Natural Origin: a Textbook of Pharmacognosy*, 5th Swedish Pharmaceutical Press, Stockholm.
 15. Kinghorn, A.D., 2001. *Pharmacognosy in the 21st century*. *J. Pharm. Pharmacol.* 53(2): 135–148.
 16. Butler, M. S. 2004. The role of natural product chemistry in drug discovery. *J. Nat. Prod.* 67(12): 2141– 2153.
 17. Haider, Z., M.A. Sheikh, M. Shahid, A. Ahmad and S.M. Ali. 2001. Antihepatotoxic evaluation of *Butea monbosperma* against liver damage induced by Rifampicin and paracetamol in chicks. *J. Biochem. Mol. Biol.* 35:41–47.
 18. Wu, F., M. Yan, Y. Li, S. Chang, X. Song, Z. Zhou and W. Gong. 2003. cDNA cloning expression and mutagenesis of a PR-10 protein SPE-16 from the seeds of *Pachyrrhizuserosus*. *Biochem. Biophys.* 312:761-766.
 19. Philipeon, J. D. 2001. *Phytochemistry and medicinal plants*. *Phytotherapy.* 56: 237-243.
 20. Kong, J. M., N. K. Goh, L. S. Chia and T. F. Chia. 2003. Recent advances in traditional plants drugs and orchids. *Acta PharmacologiaScinc.* 24: 7-21.
 21. Westh, H., C.S. Zinn and V.T. Rosdah. 2004. An international multicenter study

- of antimicrobial consumption and resistance in *Staphylococcus aureus* isolates from 15 hospitals in 14 countries. *Microb. Drug Resist.* 10:169-176.
22. Bandow, J.E., H. Brotz and L.I.O. Leichert. 2003. Proteomic approach to understanding antibiotic action. *Antimicrob. Agents Chemother.* 47:948-955.
23. Rojas, R., B. Bustamante and J. Bauer. 2003. Antimicrobial activity of selected Peruvian medicinal plants. *J. Ethnopharmacol.* 88:199-204.
24. Benkeblia, N. 2004. Antimicrobial activity of essential oil extracts of various onions (*Allium cepa*) and garlic (*Allium sativum*). *Lebensm-Wissu-Technol.* 37:263-268.
25. Iwu, M. W., A. R. Duncan and C. O. Okunji. 1999. New antimicrobials of plant origin. In: J. Janick (Ed). *Perspectives in New Crops and New Uses*,ASHS Press, Alexandria V.A. Pp. 457-462.
26. Gupta. R., B. Gabrielsen and F. M. Ferguson¹. 2005. Nature's Medicines: Traditional Knowledge and Intellectual Property Management. Case Studies from the National Institutes of Health (NIH), USA *Current Drug Discovery Technologies.* 2: 203-219.
27. Lesney, M. S. 2004. Nature's Pharmaceuticals: Natural Products from Plants Remain at the Core of Modern Medicinal Chemistry. *TCAW.* 13(7):26-31.
28. Clark A. M., Natural products as a source for New Drugs. *Pharmaceutical Research* 1996; 13(8): 1133-1141.
29. Patwardhan B., Vaidya A. D. B., Chorghade M. Ayurveda and Natural Products Drugs Discovery. *Current Science*, 2004; 86(6): 789-799.
30. Akerele O. Nature's Medicinal Bounty: Don't throw it Away. *World Health Forum* 1993; 14: 390-95.
31. Lombardino, J. G. and J. A. Lowe. 2004. The role of the medicinal chemist in drug discovery—then and now. *Nat. Rev. Drug Discov.* 3(10): 853–862.
32. Griggs, B. 1981. *Green Pharmacy, a history of herbal medicine*; J.Norman& Hobhouse Ltd.; London.
33. Okigbo, R.N. and A. N. Ajalie. 2005. Inhibition of some Human pathogens with Tropical Plant extracts. *Int. J. Mol. Med.* 1(1): 34-41.
34. WHO, 2002. Traditional medicine strategy 2002-2005. WHO publications (2002) pp. 1-6.

35. Bader, A., F. Martini, G. R. Schinella, J. L. Rios and J. M. Prieto. 2015. Modulation of cox-1, 5-, 12-and 15-lox by popular herbal remedies used in southern Italy against psoriasis and other skin diseases. *Phytotherapy Research*. 29(1): 108-113.
36. Shoemaker, M., B. Hamilton, S.H. Dairkee, I. Cohen and M.J. Campbell. 2005. In vitro Anticancer Activity of Twelve Chinese Medicinal Herbs. *Phytother. Res.* 19:649-651.
37. Pezzuto, J.M. 1997. Plant-derived anticancer agents. *Biochem. Pharmacol.* 53: 121-133.
38. Rai, M. and D. Mares. 2003, Plant-derived antimycotics: current trends and future prospects. Food Products Press, Haworth Press, New York, 587p.
39. Newman, D.J., Cragg, G.M. and K.M. Snader. 2003. Natural products as sources of new drugs over the period 1981–2002. *J. Nat. Prod.* 66(7): 1022–1037.
40. Lucca, A.J.D. and T.J. Walsh. 2000. Antifungal peptides: Novel therapeutic compounds against emerging pathogens. *Antimicrob. agents chemother.* 43:1-11
41. Ahmad, I., Z. Mehmood and F. Mohammad. 1998. Screening of some Indian medicinal plants for their antimicrobial properties. *J. Ethnopharmacol.* 62: 183-193.
42. Ahmad, I. and A.Z. Beg. 2001. Antimicrobial and phytochemical studies on 45 Indian medicinal plants against multidrug resistant human pathogens. *J. Ethnopharmacol.* 74: 113-123.
43. Bruneton, J. 1995. Pharmacognosy, Phytochemistry, Medicinal plants. France: Lavoisier Publishing Co., pp. 265-380.
44. Vaidya, A.B. 1994. Terminalia arjuna in cardiovascular therapy. *J. Assoc. Physicians India.* 42: 281–282.
45. Vlietinck, A.J., L. Van Hoof, J. Totte, A. Lasure, D.V. Berghe, P.C. Rwangabo and J. Mvukiyumwami. 1995. Screening of hundred Rwandese medicinal plants for antimicrobial and antiviral properties. *J. Ethnopharmacol.* 46: 31-47.
46. Kinghorn, A.D., 2001. Pharmacognosy in the 21st century. *Journal of Pharmacy and Pharmacology* 53 (2), 135–148.
47. Newman, D.J., Cragg, G.M., Snader, K.M., 2000. The influence of natural products upon drug discovery. *Natural Product Reports* 17 (3), 215 – 234.

48. Newman, D.J., Cragg, G.M., Snader, K.M., 2003. Natural products as sources of new drugs over the period 1981 – 2002. *Journal of Natural Products* 66 (7), 1022 – 1037.
49. Butler, M.S., 2004. The role of natural product chemistry in drug discovery. *Journal of Natural Products* 67 (12), 2141–2153.
50. Van Agtmael, M.A., Eggelte, T.A., van Boxtel, C.J., 1999. Artemisinin drugs in the treatment of malaria: from medicinal herb to registered medication. *Trends in Pharmacological Sciences* 20 (5), 199 – 205.
51. Graul, A.I., 2001. The year's new drugs. *Drug News and Perspectives* 14 (1), 12 – 31.
52. Heinrich, M., Teoh, H.L., 2004. Galanthamine from snowdrop—the development of a modern drug against Alzheimer's disease from local Caucasian knowledge. *Journal of Ethnopharmacology* 92 (2 – 3), 147 – 162.
53. Pirttila, T., Wilcock, G., Truyen, L., Damaraju, C.V., 2004. Long-term efficacy and safety of galantamine in patients with mild-to-moderate Alzheimer's disease: multicenter trial. *European Journal of Neurology* 11 (11), 734 – 741.
54. Frantz, S., Smith, A., 2003. New drug approvals for 2002. *Nature Reviews Drug Discovery* 2 (2), 95 – 96.
55. Hall, M.G., Wilks, M.F., Provan, W.M., Eksborg, S., Lumholtz, B., 2001b. Pharmacokinetics and pharmacodynamics of NTBC (2-(2-nitro-4-fluoromethylbenzoyl)-1, 3-cyclohexanedione) and mesotrione, inhibitors of 4-hydroxyphenyl pyruvate dioxygenase (HPPD) following a single dose to healthy male volunteers. *British Journal of Clinical Pharmacology* 52 (2), 169 – 177.
56. Mitchell, G., Bartlett, D.W., Fraser, T.E., Hawkes, T.R., Holt, D.C., Townson, J.K., Wichert, R.A., 2001. Mesotrione: a new selective herbicide for use in maize. *Pest Management Science* 57 (2), 120 – 128.
57. Mundy, C., Kirkpatrick, P., 2004. Tiotropium bromide. *Nature Reviews Drug Discovery* 3 (8), 643.
58. Frantz, S., 2005. 2004 approvals: the demise of the blockbuster? *Nature Reviews Drug Discovery* 4 (2), 93 – 94.
59. Barnes, P.J., Belvisi, M.G., Mak, J.C., Haddad, E.B., O'Connor, B., 1995.

- Tiotropium bromide (Ba 679 BR), a novel long-acting muscarinic antagonist for the treatment of obstructive airways disease. *Life Sciences* 56 (11–12), 853–859.
60. Dewick, P.M., 2002. *Medicinal Natural Products: a Biosynthetic Approach*, 2nd ed. John Wiley and Sons, Chichester, England.
61. Barnes, P.J., 2002. New treatments for COPD. *Nature Reviews Drug Discovery* 1 (6), 437–446.
62. Ozdemir, V.; Hekim, N. Birth of industry 5.0: Making sense of big data with artificial intelligence, “the internet of things” and next-generation technology policy. *Omics* 2018, 22, 65–76.
63. Özdemir, V. Omics 2.0: An accelerator for global science, systems medicine and responsible innovation. *Omics* 2015, 19, 579–580.
64. Wall, M.E.; Wani, M.C.; Brown, D.M.; Fullas, F.; Olwald, J.B.; Josephson, F.F.; Thornton, N.M.; Pezzuto, J.M.; Beecher, C.W.; Farnsworth, N.R.; et al. Effect of tannins on screening of plant extracts for enzyme inhibitory activity and techniques for their removal. *Phytomedicine* 1996, 3, 281–285.
65. Eldridge, G.R.; Vervoort, H.C.; Lee, C.M.; Cremin, P.A.; Williams, C.T.; Hart, S.M.; Goering, M.G.; O’Neil-Johnson, M.; Zeng, L. High-throughput method for the production and analysis of large natural product libraries for drug discovery. *Anal. Chem.* 2002, 74, 3963–3971.
66. Wu, S.; Liang, J. Counter-current chromatography for high throughput analysis of natural products. *Comb. Chem. High Throughput Screen.* 2010, 13, 932–942.
67. Harvey, A.L.; Edrada-Ebel, R.; Quinn, R.J. The re-emergence of natural products for drug discovery in the genomics era. *Nat. Rev. Drug Discov.* 2015, 14, 111–129.
68. Bugni, T.S.; Richards, B.; Bhoite, L.; Cimbor, D.; Harper, M.K.; Ireland, C.M. Marine natural product libraries for high-throughput screening and rapid drug discovery. *J. Nat. Prod.* 2008, 71, 1095–1098.
69. Koehn, F.E. High impact technologies for natural products screening. In *Natural Compounds as Drugs Volume I*; Birkhäuser: Basel, Switzerland, 2008; Volume 65, pp. 175–210.
70. Wong, W.R.; Oliver, A.G.; Linington, R.G. Development of antibiotic activity

- profile screening for the classification and discovery of natural product antibiotics. *Chem. Biol.* 2012, 19, 1483–1495.
71. He, G.; Yin, Y.; Yan, X.; Wang, Y. Semi-bionic extraction of effective ingredient from fishbone by high intensity pulsed electric fields. *J. Food Process Eng.* 2017, 40, e12392.
72. Yoshioka, T.; Nagatomi, Y.; Harayama, K.; Bamba, T. Development of an analytical method for polycyclic aromatic hydrocarbons in coffee beverages and dark beer using novel high-sensitivity technique of supercritical fluid chromatography/mass spectrometry. *J. Biosci. Bioeng.* 2018.
73. Hofstetter, R.; Fassauer, G.M.; Link, A. Supercritical fluid extraction (SFE) of ketamine metabolites from dried urine and on-line quantification by supercritical fluid chromatography and single mass detection (on-line SFE-SFC-MS). *J. Chromatogr. B* 2018, 1076, 77–83.
74. Morales, D.; Piris, A.J.; Ruiz-Rodriguez, A.; Prodanov, M.; Soler-Rivas, C. Extraction of bioactive compounds against cardiovascular diseases from *Lentinula edodes* using a sequential extraction method. *Biotechnol. Prog.* 2018.
75. Joana Gil-Ch ávez, G.; Villa, J.A.; Fernando Ayala-Zavala, J.; Basilio Heredia, J.; Sepulveda, D.; Yahia, E.M.; González-Aguilar, G.A. Technologies for extraction and production of bioactive compounds to be used as nutraceuticals and food ingredients: An overview. *Compr. Rev. Food Sci. Food Saf.* 2013, 12, 5–23.
76. De Moraes, S.R.; Oliveira, T.L.; de Oliveira, L.P.; Tresvenzol, L.M.; da Conceicao, E.C.; Rezende, M.H.; Fiuza, T.S.; Costa, E.A.; Ferri, P.H.; de Paula, J.R. Essential oil composition, antimicrobial and pharmacological activities of *Lippiasidoidescham.* (verbenaceae) from Sao Goncalo do Abaete, Minas Gerais, Brazil. *Pharmacogn. Mag.* 2016, 12, 262–270.
77. Gan, Z.; Liang, Z.; Chen, X.; Wen, X.; Wang, Y.; Li, M.; Ni, Y. Separation and preparation of 6-gingerol from molecular distillation residue of Yunnan ginger rhizomes by high-speed counter-current chromatography and the antioxidant activity of ginger oils in vitro. *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.* 2016, 1011, 99–107.
78. Zhang, L.; Mei, J.; Xie, Y.; Li, M.; Liu, D.; He, C. Application of membrane

- separation technology in extraction process of Chuanxiong Chatiao granules. *Zhongguo Zhong yao za zhi = Zhongguozhongyaozazhi = China J.Chin. Mater. Med.* 2012, 37, 934–936.
79. Williams, S.; Oatley, D.; Abdrahman, A.; Butt, T.; Nash, R. Membrane technology for the improved separation of bioactive compounds. *Procedia Eng.* 2012, 44, 2112–2114.
80. Wang, H.; Jiang, Y.; Ding, M.; Li, J.; Hao, J.; He, J.; Wang, H.; Gao, X.M.; Chang, Y.X. Simultaneous determination and qualitative analysis of six types of components in Naoxintong capsule by miniaturized matrix solid-phase dispersion extraction coupled with ultra high-performance liquid chromatography with photodiode array detection and quadrupole time-of-flight mass spectrometry. *J. Sep. Sci.* 2018.
81. Zhang, L.; Ge, Y.; Li, J.; Hao, J.; Wang, H.; He, J.; Gao, X.M.; Chang, Y.X. Simultaneous determination of columbianetin-beta-d-glucopyranoside and columbianetin in a biological sample by high-performance liquid chromatography with fluorescence detection and identification of other columbianetin-beta-d-glucopyranoside metabolites by ultra high-performance liquid chromatography coupled with quadrupole-time of flight mass spectrometry. *J. Pharm. Biomed. Anal.* 2018, 153, 221–231.
82. Manglik, A.; Kruse, A.C.; Kobilka, T.S.; Thian, F.S.; Mathiesen, J.M.; Sunahara, R.K.; Pardo, L.; Weis, W.I.; Kobilka, B.K.; Granier, S. Crystal structure of the micro-opioid receptor bound to a morphinan antagonist. *Nature* 2012, 485, 321–326.
83. Edwards, G. Forces of habit: Drugs and the making of the modern world. *Addiction* 2002, 97, 608–609.
84. Thomford, N.E.; Mkhize, B.; Dzobo, K.; Mpye, K.; Rowe, A.; Parker, M.I.; Wonkam, A.; Skelton, M.; September, A.V.; Dandara, C. African lettuce (*Launaeataraxacifolia*) displays possible anticancer effects and herb-drug interaction potential by CYP1A2, CYP2C9, and CYP2C19 inhibition. *Omics* 2016, 20, 528–537.
85. Zhao, L.; Li, C.; Zhang, Y.; Wen, Q.; Ren, D. Phytochemical and biological

- activities of an anticancer plant medicine: *Bruceajavanica*. *Anti-Cancer Agents Med. Chem.* 2014, 14, 440–458.
86. Wen, M.C.; Wei, C.H.; Hu, Z.Q.; Srivastava, K.; Ko, J.; Xi, S.T.; Mu, D.Z.; Du, J.B.; Li, G.H.; Wallenstein, S.; et al. Efficacy and tolerability of anti-asthma herbal medicine intervention in adult patients with moderate-severe allergic asthma. *J. Allergy Clin. Immunol.* 2005, 116, 517–524.
87. Srivastava, K.; Sampson, H.A.; Charles, W.; Emala, S.; Li, X.-M. The anti-asthma herbal medicine ashmi acutely inhibits airway smooth muscle contraction via prostaglandin e2 activation of ep2/ep4 receptors. *Am. J. Physiol.-Lung Cell. Mol. Physiol.* 2013, 305, L1002–L1010.
88. Yang, N.; Liang, B.; Srivastava, K.; Zeng, J.; Zhan, J.; Brown, L.; Sampson, H.; Goldfarb, J.; Emala, C.; Li, X.M. The *Sophora flavescens* flavonoid compound trifolirhizin inhibits acetylcholine induced airway smooth muscle contraction. *Phytochemistry* 2013, 95, 259–267.
89. Chan, K.; Shaw, D.; Simmonds, M.S.; Leon, C.J.; Xu, Q.; Lu, A.; Sutherland, I.; Ignatova, S.; Zhu, Y.P.; Verpoorte, R.; et al. Good practice in reviewing and publishing studies on herbal medicine, with special emphasis on traditional Chinese medicine and Chinese materia medica. *J. Ethnopharmacol.* 2012, 140, 469–475.
90. Skroza, D.; Generali'c Mekini'c, I.; Svilovi'c, S.; Šimat, V.; Katalini'c, V. Investigation of the potential synergistic effect of resveratrol with other phenolic compounds: A case of binary phenolic mixtures. *J. Food Compos. Anal.* 2015, 38, 13–18.
91. Chusri, S.; Siriyong, T.; Na-Phatthalung, P.; Voravuthikunchai, S.P. Synergistic effects of ethnomedicinal plants of *Apocynaceae* family and antibiotics against clinical isolates of *Acinetobacter baumannii*. *Asian Pac. J. Trop. Med.* 2014, 7, 456–461.
92. Sharma, G.; Tyagi, A.K.; Singh, R.P.; Chan, D.C.; Agarwal, R. Synergistic anti-cancer effects of grape seed extract and conventional cytotoxic agent doxorubicin against human breast carcinoma cells. *Breast Cancer Res. Treat.* 2004, 85, 1–12.

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93. Van Der Heijden, R., Jacobs, D.I., Snoeijer, W., Hallard, D., Verpoorte, R., 2004. The Catharanthus alkaloids: pharmacognosy and biotechnology. *Current Medicinal Chemistry* 11 (5), 607 – 628.
94. Okouneva, T., Hill, B.T., Wilson, L., Jordan, M.A., 2003. The effects of vinflunine, vinorelbine, and vinblastine on centromere dynamics. *Molecular Cancer Therapeutics* 2 (5), 427 – 436.
95. Reichert, J.M., 2003. Trends in development and approval times for new therapeutics in the United States. *Nature Reviews Drug Discovery* 2 (9), 695 – 702.
96. Dickson, M., Gagnon, J.P., 2004. Key factors in the rising cost of new drug discovery and development. *Nature Reviews Drug Discovery* 3 (5), 417 – 429.
97. Do, Q.T., Bernard, P., 2004. Pharmacognosy and reverse pharmacognosy: a new concept for accelerating natural drug discovery. *IDrugs* 7 (11), 1017 – 1027
98. Koehn, F.E., Carter, G.T., 2005. The evolving role of natural products in drug discovery. *Nature Reviews Drug Discovery* 4 (3), 206 – 220.
99. Rosenthal, J., 2002. Curtain has fallen on hopes of legal bioprospecting. *Nature* 416 (6876), 15.
100. Soejarto, D.D., Gyllenhaal, C., Fong, H.H., Xuan, L.T., Hiep, N.T., Hung, N.V., Bich, T.Q., Southavong, B., Sydara, K., Pezzuto, J.M., 2004. The UIC ICBG (University of Illinois at Chicago International Cooperative Biodiversity Group) Memorandum of Agreement: a model of benefit-sharing arrangement in natural products drug discovery and development. *Journal of Natural Products* 67 (2), 294 – 299.
101. Knowles, J., Gromo, G., 2003. Target selection in drug discovery. *Nature Reviews Drug Discovery* 2 (1), 63 – 69.
102. Kramer, R., Cohen, D., 2004. Functional genomics to new drug targets. *Nature Reviews Drug Discovery* 3 (11), 965 – 972.
103. Walters, W.P., Namchuk, M., 2003. Designing screens: how to make your hits a hit. *Nature Reviews Drug Discovery* 2 (4), 259 – 266.
104. Eldridge, G.R., Vervoort, H.C., Lee, C.M., Cremin, P.A., Williams, C.T., Hart, S.M., Goering, M.G., O'Neil-Johnson, M., Zeng, L., 2002. High-throughput method for the production and analysis of large natural product libraries for

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3007-3197

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3007-3189

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- drug discovery. *Analytical Chemistry* 74 (16), 3963 – 3971.
105. Pellecchia, M., Sem, D.S., Wuthrich, K., 2002. NMR in drug discovery. *Nature Reviews Drug Discovery* 1 (3), 211 – 219.
106. Glish, G.L., Vachet, R.W., 2003. The basics of mass spectrometry in the twenty-first century. *Nature Reviews Drug Discovery* 2 (2), 140 – 150.
107. Blundell, T.L., Jhoti, H., Abell, C., 2002. High-throughput crystallography for lead discovery in drug design. *Nature Reviews Drug Discovery* 1 (1), 45–54.