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Plant active metabolites: A new paradigm in the treatment of Hypertension (a brief description of Indian Pharmacopoeia – 2022 herbal monographs)

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Hypertension is a significant public health problem worldwide. Nearly two-thirds of all hypertensive patients live in developing and under-developed countries, creating a considerable burden of hypertension. India is among the countries which spend more than one-third of all income on cardiovascular diseases and hypertension. Although several modern medications are available to control the disease symptoms, their expense and side effects restrict their public use. More than 80% of the world's population relies on traditional treatment, which is used recklessly without any restrictions or proof thereof. Indian Pharmacopoeia is working diligently towards standardising herbal drugs and plant-derived pharmaceuticals, i.e., Phyto-pharmaceuticals, to regulate their usage. The present article focuses on the standardisation of marker compounds of different indigenous anti-hypertensive medicinal plants, which can be used as bioactive markers in phytopharmaceutical drug development. The study includes consolidated information about the important anti-hypertensive biomarkers and their identification and assay methodology.

Keywords: Clinical efficacy, Herbal monographs, Hypertension, Indian Pharmacopoeia – 2022, Marker compounds

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Introduction

The burden of cardiovascular disease (CVD) is increasing worldwide[1]. The disease has been attributed to more than 17 million deaths globally, to which India contributes approximately 28.1% of the total deaths[2]. Though allopathic medications are commonly available for disease treatment, their high cost and side effects make them unpopular among the general public. Due to the poor healthcare system, there is little or no disease awareness. This makes the treatment and its prevention extremely difficult. The sedentary lifestyle and rapid urbanisation in developing countries add to the woes and cause rapid spread. The estimated prevalence of awareness, treatment and control of blood pressure (BP) are 25.3, 25.1, and 10.7% for rural Indians and 42.0, 37.6, and 20.2% for urban Indians respectively[3]. A new, effective, and in-expensive anti-hypertensive drug with minimum side effects is the need of the hour. Natural products derived from plants are known for their vast pharmacological activities and have been developed into medicines and herbal formulations for therapeutic purposes. In recent years, herbal drugs have significantly impacted cardiovascular disease management as shown by preclinical and clinical studies[4–6]. Though their usage is globally accepted, appropriate standardisation of the quality of such herbal drugs needs to be maintained to ensure efficacy[7]. For this, a uniform method for qualitative and quantitative identification characterisation of active biomarkers derived from plants is required to be followed across the country. Therefore, Indian Pharmacopoeia Commission (IPC), in its current edition, has attempted to ensure the standardisation of bioactive markers in various herbal drugs responsible for the management of cardiovascular diseases. Indian Pharmacopoeia – 2022 (IP-2022) as herbal monographs. IP-2022 describes the standards for pharmaceuticals, vaccines, radiopharmaceuticals, phytopharmaceuticals, and herbal drugs. IP–2022 has developed 183 herbal monographs and 7 Phytopharmaceuticals Ingredient (PPI) monographs (Fig. 1 & 2) and standardised 14 marker compounds of herbal drugs (Table 1). This article provides detailed information on the standardised methods

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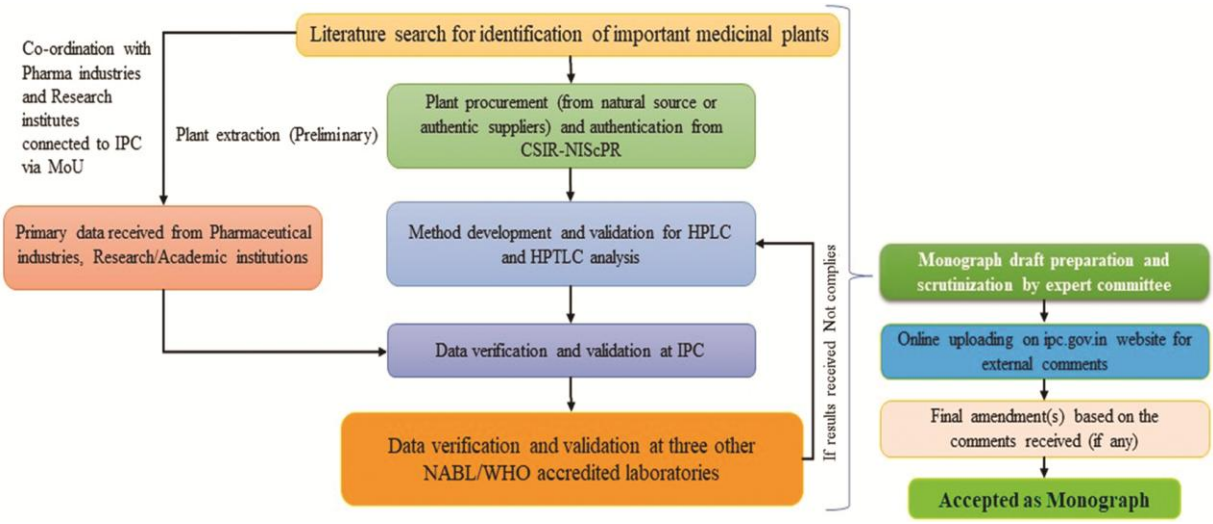

Fig. 1 — Process of development of herbal and phytopharmaceuticals ingredient monographs at Indian Pharmacopoeia Commission.

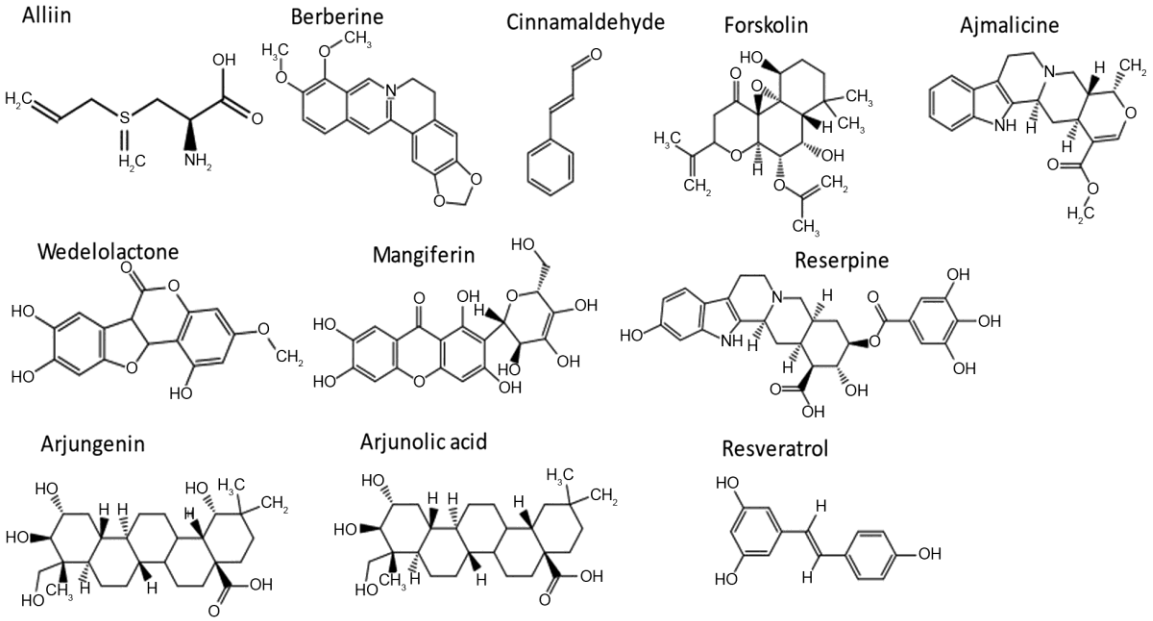

Fig. 2 — Chemical structures of the phytochemicals as a potential anti-hypertensive marker.

developed in IP–2022, for plants possessing anti-hypertensive marker compounds and aims to elaborate the standard for marker compounds for clinical use.

Anti-hypertensive marker compounds

Alliin

Alliin, also known as S-allyl-cysteine sulfoxide, is a marker compound present in *Allium sativum* (garlic), which is not less than 0.2% (w/w) in the plant[8]. *Allium sativum* contains more than 20 kinds of sulphide compounds, out of which a few Sulphur-containing amino acids are produced by garlic with diverse functions. The main feature of garlic products is the distinctive flavour formed by complex biochemical reactions due to the presence of Sulphur-containing non-volatile amino acids (thiosulfates). *Alliin* is one of the most predominant thiosulfates in *A. sativum*, a precursor molecule responsible for its flavour. The compound has been reported to be a potent antioxidant with cardioprotective and neuroprotective actions[9–11]. In addition, it helps decrease serum levels of glucose, insulin, triglycerides, and uric acid, as well as insulin resistance and reduces cytokine levels. A meta-analysis including 20 clinical trials suggested garlic to

Table 1 — List of marker compounds are their source plants responsible for anti-hypertensive activity.

Marker Compounds	Source plant	Part	Monograph in IP - 2022	Total content (w/w) As per IP - 2022	Retention time as per HPLC method in IP 2022 (min)	PubChem CID
Allin	*Allium sativum* (Fam. Amaryllidaceae)	Bulb	Lahsuna	NLT 0.20	8.5	121922
Berberine	*Berberis aristata* (Fam. Berberidaceae)	Stem	Dharuharidra	NLT 0.70	11	2353
Cinnamaldehyde	*Cinnamomum verum, Cinnamomum zeylanicum, Cinnamomum tamala* (Fam. Lauraceae)	Bark	Dalchini	NLT 0.36	6 (GC method)	637511
Wedelolactone	*Eclipta alba* (Fam. Asteraceae)	Arial part	Bhringraj	NLT 1.10	9.5	5281813
Forskolin	*Coleus forskohlii* (Fam. Lamiaceae)	Roots	Patha	NLT 90-120	15	47936
Mangiferin	*Mangifera indica* (Fam. Anacardiaceae)	Fruit	Amra	NLT 1.50	8	5281647
Reserpine	*Rauwolfia serpentine* (Fam. Apocynaceae)	Roots	Sarpgandha	0.15-0.20	32.5	5770
Ajmalicine	*Rauwolfia serpentine* (Fam. Apocynaceae)	Roots	Sarpgandha	85-115	9	441975
Arjungenin	*Terminalia arjuna* (Fam. Combretaceae)	Bark	Arjun	0.02	6	12444386
Arjunolic acid	*Terminalia arjuna* (Fam. Combretaceae)	Bark	Arjun	90-110	14	73641
Resveratrol	*Myristica fragrans* (Fam. Myristicaceae)	Fruit/Nut	Nutmeg oil	NLT 0.05	16	445154

be superior to placebo in lowering the blood pressure (BP) in hypertensive patients on an average by 8-9 mmHg in systolic BP (SBP) and 6-7 mmHg in diastolic BP (DBP)[12–14]. The relaxation of vascular smooth muscle cells is an element of the physiological mechanisms for lowering BP. Reduced responsiveness of blood vessels to relax from constriction following autonomic nervous, endocrine/ proteinoid, or shear stress signaling is thought to be an important factor in the pathophysiology of hypertension, as indicated by experimental and clinical evidence[15]. As per IP guidelines, alliin is identified by Thin Layer Chromatography (TLC) and assayed by using the method of high-performance chromatography using stainless steel column 25 cm x 4.6 mm packed with octadecylsilane bonded to porous silica 5 µm and mobile phase contains 0.1 per cent v/v phosphoric acid prepared by diluting 1 mL of orthophosphoric acid to 1000 mL with water, flow rate 0.5 mL per minute, detection at 210 nm, injection volume 20 µL. The retention time of Allin, with the method mentioned above, comes within 8-9 min.

Berberine

Berberine (5,6-dihydro-9,10-dimethoxybenzo[g]-1,3-benzodioxolo[5,6a]-quinolizinium) is an alkaloid commonly present in *Berberis aristata*. IP describes the limits for berberine content as not less than 0.70% (w/w) found in the roots, identified by TLC, and assayed by HPLC[8]. *B. aristata* is also useful in treating cardiovascular diseases[16]. It is speculated that *B. aristata* fruit extract exhibits a positive inotropic action in the isolated cardiac tissues. The active principles of the plant are known to cause a selective inotropic effect by producing a modulatory effect on actin myosin co-operativity, which is one of its mechanisms of action[17]. The biochemical study on *B. aristata* revealed a significant reduction in serum cholesterol, triglycerides and low-density lipoprotein levels was noted with an increase in fibrinogen and thrombin time in a study performed on healthy rabbits of either sex. The clinical effects of BBR treatment on Flow Mediated Vasodilation (FMD) have also been recently demonstrated in a clinical, double-blind, placebo-controlled study, in which BBR was administered in combination with other recognised hypolipidemic nutraceutical agents such as policosanols and red yeast rice (RYR). This study demonstrated that the treatment significantly improved FMD in a population of hyper-cholesterolemic subjects[18]. Besides the effects on endothelial function, several animal and clinical studies have demonstrated the therapeutic potential of BBR as supportive in the treatment of hypertension,

atherosclerosis and heart disease, including left ventricular remodelling[19]. The HPLC method described in IP – 2022 consists of two methods; *Method 1*- Stainless steel HPLC column packed with C18 silica gel; (25cm × 4.6 mm in length and 5 µm pore size). The mobile phase used for compound elution was phosphate buffer solution (prepared by 0.136 g potassium di-hydrogen orthophosphate in 1L MiliQ water)as mobile phase (A) and Acetonitrile as mobile phase (B) with a gradient program as follows: 0-25 min, 80-20% A-B; 25-26 min, 50-50% A-B; 26-30 min, 80-20% A-B and the post-run (4 min) for equilibrium at a flow rate of 1.5 mL/min at wavelength 310 nm. The injection volume was 20 µL. *Method 2*- Stainless steel HPLC column packed with C18 silica gel; (15 cm × 4.6 mm in length and 5 µm pore size). The mobile phase used for compound elution was 73 volumes of phosphate buffer solution (prepared by 0.136 g potassium di-hydrogen orthophosphate in 1L MiliQ water) and 27 volumes of acetonitrile, isocratic elution with a flow rate is 1.2 mL per minute. The total run time is 30 min; the detection wavelength is set at 235 nm, and the retention time is around 11 min.

Cinnamon leaf and bark oil (*Cinnamaldehyde*)

IP describes the bark of *Cinnamomum verum*, *Cinnamomum tamala*, and *Cinnamomum zeylanicum* consisting of essential oil, identified and assayed by Gas chromatography (GC) (Table 1). Several studies have reported the anti-hypertensive activity of Cinnamon oil. Acute intravenous administration of *C. zeylanicum* extracts (5, 10 and 20 mg/kg) to L-NAME-induced hypertensive rats provoked a long-lasting decrease in blood pressure. Mean arterial blood pressure decreased by 12.5%, 26.6% and 30.6% at 5, 10 and 20 mg/kg doses, respectively[20,21]. According to a clinical trial study, *cinnamaldehyde* in Cinnamon oil produces a hypotensive effect by peripheral vasodilatation in anaesthetised dogs and guinea pigs. The study was conducted on 38 subjects, of which 33 showed no adverse effect[20]. The side effects reported were mild gastrointestinal disorder and mild allergy, mostly self-limiting. Acute administration of *Cinnamomum zeylanicum* aqueous extract (CZA) induces the hypotensive/anti-hypertensive effects in the experimental animal models used, and this might be mediated via cholinergic and adrenergic mechanisms; its direct vasorelaxant effect may also contribute to the reduction in high blood pressure[21]. In addition, the vasorelaxant effect of CZA might be mediated, at least in part, by increasing the release of nitric oxide from endothelial cells and through the activation of KATP channels in vascular smooth muscle[22]. The hypotensive/anti-hypertensive action of *Cinnamomum zeylanicum* described in this work provides scientific evidence for its use in managing hypertension[20]. Twenty-eight subjects completed the three months follow-up. Both systolic and diastolic blood pressure reduced significantly during the 1st month, and this reduction was sustained throughout the follow-up. Full blood count, renal function tests, liver function tests, fasting blood glucose, HDL-c, VLDL-d and triglycerides remained within the normal range without significant alteration during the 3 months. A significant reduction in the TC ($P < 0.05$) and LDL-c ($P < 0.001$) was noted at the end of the 3 months follow-up period. There was no report of serious adverse effects (including hypersensitivity). In two participants, dyspepsia necessitated the discontinuation of study participation. Drug compliance was between 85 and 95% during the study period[23]. The GC detection of Cinnamon oil was done by a 60 m × 0.25 mm capillary column coated with macrogol 20000. The temperature of the column was set at 60°C for 10 min and then increased to 190°C at a rate of 2°C/min for 125 min. The inlet port was set at 200 degrees, and the detector at 240 degrees. Detection was done by flame ionisation detector, at a flow rate of 1.5 mL per minute, using helium as carrier gas. The sample injection volume was 0.2 µL with a split ratio of 1:100[8].

Wedelolactone

This marker compound is found in *Eclipta alba*, *chemically* classified under *coumestan* (7-methoxy-5,11,12-trihydroxy-coumestan). Wedelolactone is identified by TLC and assayed by HPLC using a method described in the effect of administration of dried *E. alba* leaf powder (3 g per day) has been studied in mildly hypertensive subjects. Subjects were given six capsules (500 mg powder per capsule) in three doses per day for 60 days. When compared with placebo control groups, the results showed that *Eclipta-alba* supplemented group showed a marked reduction in mean arterial pressure by 15%, total cholesterol (17%), low-density lipoprotein fraction (24%), triglycerides (14%), very-low-density lipoprotein fraction (14%), and plasma lipid peroxides (18%). There was a marked increase in urine volume (34%), urine sodium (24%), serum vitamin C (17%), and serum tocopherols (23%) in the *Eclipta-*

administered group. These findings indicate that leaf powder has diuretic, hypotensive, and hypocholesterolemia properties and helps alleviate oxidative stress-induced complications in hypertensives[24,25]. The detection of *wedelolactone* by HPLC was done by using stainless steel column of 25cm × 4.6mm; 5 µm, packed with octadecylsilane bonded to porous silica. The sample injection volume was 20 µL, while the mobile phase was 35 volumes of acetonitrile and 60 volumes of 0.1 per cent v/v solution of orthophosphoric acid (prepared by diluting 1 mL of orthophosphoric acid to 1000 mL with water) at 1 mL/min flow rate and detection at 249 nm[8]. The retention time of Wedelolactone with the above-given method comes within 9-10 min.

Forskolin

IP describes the forskolin as a diterpene compound evaluated qualitatively and quantitatively from the root and stem of *Coleus forskohlii*, and the dried roots contain not less than 90-120% of forskolin[8]. It is identified by TLC and assayed using the HPLC. The assay method is developed by 25 cm 0.46 mm packed with octadecylsilane bonded to porous silica 5 µm utilising a mixture of 55 volumes of *water* and 45 volumes of acetonitrile, the flow rate is 1 mL/min and detection at 210 nm with injection volume 20 µL.

This naturally derived compound is known to interact with the adenylyl cyclase enzyme, which upregulates the production of cyclic Adenosine Monophosphate (cAMP). This leads to an increase in the level of intracellular cAMP, in turn increasing the signal transmitters, which usually gets decreased in cardiovascular diseases, diabetes, obesity, asthma, and other chronic disorders. Several clinical trials using forskolin effects on patients with conditions such as asthma, cystic fibrosis, chronic obstructive pulmonary disease (COPD), metabolic syndrome, obesity and glaucoma have proved the usefulness of the compound[26–30].

Mangiferin

IP describes that the bark of *Mangifera indica* contains *mangiferin*, not less than 1.5%. As per IP 2022, Mangiferin is identified by TLC and assayed by HPLC using column 25 cm x 4.6 mm packed with octadecylsilane bonded to porous silica 5 µm, 15 volumes of acetonitrile and 85 volumes of buffer having 1.36g of Potassium dihydrogen orthophosphate in 950 mL of water, adjusted pH 2.8 with orthophosphoric acid, flow rate 1 mL per minute, detection at 365 nm and injection volume 20 µL pH 2.8; with retention time at 8 min[8].

The bark of the mango tree is known to contain mangiferin protocatechic acid and catechin in high quantity[31,32]. Mangiferin, a polyphenolic antioxidant and glucosyl xanthone, has strong antioxidant, anti-lipid peroxidation, immunomodulation, cardiotonic, hypotensive, wound healing, antidegenerative and anti-diabetic activities[33]. Mangiferin was reported to significantly relieve the elevated blood pressure in hyperuricemic rats induced by potassium oxonate. Mangiferin acts by increasing NO secretion and improving endothelial function[34]. Mangiferin might improve endothelial function by relieving oxidative stress and inflammation. However, whether mangiferin exerts anti-hypertension effects in any other models, such as spontaneously hypertensive rats (SHR) or stroke-prone spontaneously hypertensive rats (SHR-SP), is still unknown[35]. However, in a research study, it has been depicted that mangiferin has its potential utility as a multitargeted compound for mixed osteoarthritic pain. The claim has been supported by preclinical evidence of clinical musculoskeletal or neuropathic pain in patients. This shows the potential of using mangiferin to reduce post-diabetic symptoms, especially in neuropathy[36–38].

Reserpine

It is an indole alkaloid in the 0.15 - 0.2 per cent w/w present in *Rauwolfia serpentina*, identified by TLC and assayed by HPLC. In HPLC with 25cm × 4.6 m packed with octadecylsilane bonded to porous silica 5 µm having mobile phase 35 volumes of acetonitrile and 65 volumes of buffer solution prepared by dissolving 6.8 g potassium dihydrogen phosphate in 1000 mL water and adjust the pH to 3.0 with dilute orthophosphoric acid, flow rate 1 mL per minute, detection at 268 nm and injection volume is 10 µL[8]. The mechanism of action of reserpine is well-researched and well-documented. Reserpine binds to protein receptors called vesicular monoamine transporters (VMATs) in the organelle membranes of specialised secretory vesicles of presynaptic neurons[39]. Reserpine prevents intracellular neurotransmitters from binding to VMAT proteins and stops secretory vesicles from taking neurotransmitters. In randomised clinical trials, the overall pooled effect demonstrated a statistically significant SBP reduction in participants taking reserpine compared with placebo (weighted mean difference (WMD) 7.92, 95% confidence interval (CI)

14.05 to 1.78). Due to significant heterogeneity across the trials, a significant effect in DBP, mean arterial pressure (MAP), and heart rate (HR) could not be found. A dose of reserpine 0.5 mg/day or greater achieved the SBP effects. None of the trials reported any withdrawals due to adverse effects[40]. The authors concluded that reserpine effectively reduced systolic blood pressure to the same degree as other first-line anti-hypertensive drugs. However, they could not make definite conclusions regarding the dose-response pattern because of the small number of trials.

Ajmalicine

Ajmalicine, also known as *δ-yohimbine or raubasine*, is an alkaloid predominantly present in *Rauwolfia serpentina* (85-115% w/w), identified by TLC and assayed using HPLC. HPLC with 25 cm x 4.6 m packed with octadecylsilane bonded to porous silica 5 µm having mobile phase 35 volumes of acetonitrile and 65 volumes of a buffer solution prepared by dissolving 6.8 g potassium dihydrogen phosphate in 1000 mL water and adjust the pH to 3.0 with dilute orthophosphoric acid, flow rate 1 mL per minute, detection at 268 nm and injection volume is 10 µL. Ajmalicine is an α-adrenergic blocking spasmolytic agent. It is also known to reverse high doses into adrenalin effects and decreases the activity of blood vessels (vasomotor) in the bulbar center. Ajmaline has an antiarrhythmic action, but it is not commonly used because of its toxicity. Based on a study on frogs, it was shown that the ajmaline group acts as a general depressant to the heart, respiration, and central nervous system, whilst the serpentine group causes paralysis of respiration, depression of nerves, and stimulation of the heart[41].

Arjungenin

Arjungenin is triterpenoid saponin, with IUPAC name as *2,3,19,23-tetrahydroxyolean12-en-28-oïc acid*. The compound can be isolated from the bark of *Terminalia arjuna* as the plant contains not less than 0.02%. In Ayurveda, it is used as *hridaya* (heart tonic), *medah hara* (reduces fat) and *raktasodhana* (purifies excess pitta) and prescribed (1-6 gm per day) dried bark. In a clinical study, patients with a history of heart failure or chronic coronary artery disease were administered the preparation of aqueous extract from the bark of *T. arjuna* at a dose of 500 mg[42]. 12 out of 16 patients showed miraculous recovery with this adjuvant therapy. It was found that the arjuna extract heals idiopathic dilated cardiomyopathy. The therapy was found safe and caused long-lasting improvements in symptoms and signs of heart failure along with improvement in left ventricular ejection phase indices with a definite improvement in the quality of life.

Arjunolic acid

Arjunolic acid (AA: *2,3,23-trihydroxyolean-12-en-28-oic* acid), is a natural chiral triterpenoid saponin, usually isolated from the bark of *Terminalia arjuna*, and also present (90-110%) in dry extract of Arjuna bark as a marketed product. The compound can easily be characterised and identified by thin-layer chromatography and HPLC. As per IP, the HPLC method developed for detecting Arjunolic acid consists of a stainless-steel column 250 mm x 4.6 mm; 5 µm, packed with silica gel, with gradient elution. The mobile phase for the gradient programming consists of (A) 70% acetonitrile in an aqueous solution; and (B) 30 % acetonitrile in an aqueous solution. The described gradient program is as follows: 0-10 min, linear gradient 30% A-70% B; 10-30 min, linear gradient 50% A-50% B; 30-50 min, linear gradient 70% A-30% B and the post-run (20 min) for equilibrium at a flow rate of 1.2 mL/min and wavelength 210 nm. The injection volume was 20 µL; the retention time at 14 min.

Arjuna tree is commonly known for its cardio-protective nature in *Charaka Samhita*, *Sushruta Samhita* and *Astang Hridayam*. The scientific studies on the tree bark and its phytoconstituents verify the information provided in the Ayurvedic texts. Arjunolic acid is one of the Arjuna tree's main phytocompound(s). It is well known for various biological functions, including cytoprotective, anti-fungal, antibacterial, anti-diabetic, diuretic and insect growth inhibitor activities. In a clinical study, 36 hypertensive patients (stage III) with increased LV mass were administered an Ayurvedic formulation of *T. arjuna*, known as *'Arjuna Kwath'* (25 mL twice a day). They observed a significant decrease in both SBP and DBP (P <0.001) in both the groups was observed, LV mass index was only significantly reduced in the atenolol-plus – '*Arjuna Kwatha*' group as compared to atenolol[43].

Resveratrol

It is a polyphenol non-flavonoid compound in strongly pigmented vegetables and fruits such as grapes, wines, peanuts, and soy. This substance has diverse biological activities, including antitumor,

antioxidant, antiviral, and Phyto-estrogenic[44,45]. The chemical moiety resveratrol was identified by TLC and assayed by HPLC in Indian Pharmacopoeia 2022. The HPLC method consists of a stainless-steel column 25cm × 4.6 mm packed with silica gel. The mobile phase was potassium di-hydrogen orthophosphate in aqueous solution (A) and acetonitrile (B) with a gradient program as follows: 0-18 min, isocratic elution100% A; 18-25 min, isocratic elution 100% A; 25-30 min, linear gradient 55-45% B; 30-33 min, linear gradient 20-80% B, and the post-run (3 min) for equilibrium at a flow rate of 1.5 mL/min and wavelength 310 nm. The injection volume was 20 μL; the retention time of Resveratrol is 16 min. A study has reported that an increase in the consumption of resveratrol improves flow-mediated dilation (FMD). Resveratrol was also found to control blood pressure, obesity, and post-menopausal symptoms, as observed in studies[45–47].

Discussion and Conclusion

Indian Pharmacopoeia has described several significant bioactive markers that are known to exhibit anti-hypertensive effects. According to the WHO guidelines, these bioactive markers are also assayed and confirmed in the standardised extracts and Botanical Reference Substances (IPBRS) using the modern analytical technique. The corresponding biomarkers are described in the herbal monographs in the IP-2022 edition. The biomarkers selected in the present article contribute significantly to trade values in global pharmaceutical industries. This accords that a well-established identification and quantification method be followed uniformly nationwide. The methodologies described above are robust, cost-effective, sophisticated and easily reproducible at industrial levels. The popularity of herbal formulations has reached new heights recently, so the demand for bulk production has exponentially increased. Most of these herbal medicines are consumed by patients as dietary supplements or complementary medicines. Many herbal extracts described above are not prescribed by medical practitioners but are taken as over-the-counter drugs, just like food supplements. Hence, it is important to stringently regulate the quality and quantity of herbal formulations for the safety and efficacy of the products.

Indian Pharmacopoeia Commission (IPC) is a regulatory body rigorously working to regulate and formulate protocols to ensure uniformity in the quality of herbal formulations. The Commission is also involved in developing Phytopharmaceutical Ingredients monographs based on the active fraction(s) isolated from the medicinal plants or its part, containing the bioactive compounds in definite concentration, duly characterised and quantified by globally recognised methodologies. The bioactivity of the isolated fractions is determined by valid *in-vitro* analysis, and their safety is studied by implementing advanced *in-silico* tools for conducting ADMET study. The bioactive compounds mentioned above will be implemented in the upcoming IP edition, and their phytopharmaceutical ingredients will be scientifically validated as anti-hypertensive agents. The information shared in the review can be used to isolate the bioactive compounds and check for the preparation quality. This will help regulate a compound's dose and purity, which could then be evaluated for its role as a prescription drug. Healthcare professionals, regulators, academicians and other stakeholders of the healthcare sector must join hands to regulate and frame protocols for such phytopharmaceuticals so that the preparations are devoid of any discrepancies and the quality and quantity of the best standard are ensured.

To delineate the toxic effects of phytopharmaceutical drugs, IPC also focuses on identifying the toxic compounds present in medicinal plants. This will help in removing unwanted side effects. IPC is currently engaged in developing and certifying the Phytopharmaceuticals Reference Standard for these anti-hypertensive marker compounds. The efforts would serve as a model to extrapolate it to other herbal formulations and drugs known for their respective effects. This review summarises the biomarker compounds specified in Indian Pharmacopeia-2022.

Conflict of interest

The authors report no conflicts of interest.

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