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EFFECT OF SEASONAL VARIATION ON SECONDARY METABOLITES OF MEDICINAL PLANTS

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ABSTRACT: Seasonal fluctuations are periodical series, and have impact on availability of active principles in medicinal plants hence, therapeutic efficacy also get influenced. The survey of several scientific studies published in scientific journals of international repute indicates this fact. The studies reported that essential oil component shows a rhythmic increase in oil production throughout the growing season and then a steady decline towards the winter hence, recommended late summer as the best collection time. In contrast other researchers concluded the winter as a best season for harvesting of essential oils containing plant parts. It is not only essential oil that influenced by the season but other important constituents like polyphenol, flavonoids, glycosides, alkaloids etc are also influenced significantly by seasons. There is no general rule for the harvesting time for better yield of specific secondary metabolites. Although several studies have been published indicating the effect of seasons on secondary metabolites but there is no compiled information representing the optimized season for the collection of pharmaceutically important constituents from different plant sources. Therefore, present review has been targeted the information of best possible season for the harvesting of plant material for the maximum output with respect to pharmaceutically important chemicals from the plants.

INTRODUCTION: Plant diversity has a considerable importance as a source of pharmaceutically active substances.[1] Environmental conditions affect not only plant growth but also influences secondary metabolites. The medicinal plants show a marked variation in active ingredients during different seasons; as these have been widely attributed to variations in environmental variables such as temperature and rainfall.[2, 3] There are several assumptions regarding the time and season for the collection of various parts of the medicinal plants like spring is suitable for the collection of bark, winter for essential oils etc.

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This review is a collection of the studies of several groups of researchers on the effect of seasonal variations on secondary metabolites content of medicinally important plants. The results of these studies may help to the researcher those are involved in exploring the plants for the isolation of valuable chemicals from the plants.

The whole article is divided in three different categories i.e. effect of seasonal variation on volatile components, non-volatile components and on pharmacological activities. In this review we aimed to compile the results of researchers those have worked in this field and reported the components of several popular plants.

Effect of seasonal variation on Volatile contents: The study carried out on the essential oils of *Pelargonium graveolens* for evaluating the impact of seasons on yield and geraniol contents. The winter was reported as the best season for the harvesting of *P.graveolens* leaves as it gave the highest content of geraniol (29.87%) content. [4]

The results of present study confirms the previous finding which describes that during summer, geranium subjected to thermal (atmospheric as well as soil) and moisture stresses ended up producing low biomass yield because of reduction in levels of photosynthesis and damaging effects of solarisation [5].

In another study, the essential oil of *Thymus serpyllum* L. was evaluated to optimize the best season for its collection. The essential oil content was found highest in summer season (0.28%) lowest (0.17% and 0.07%) during autumn and winter season whereas the highest value of thymol content was found during autumn (60.1%). This decrease of volatile oils amount in *T. serpyllum* may be due to setting of seeds during autumn that may deteriorate the oil glands.[6]

In another study, the essential oil of *Melissa officinalis* showed the variation in yield considerably from month-to-month and also reported to be influenced by the micro-environment (sun or shade) in which the plant is growing [7].

The influence of season on chemical composition of essential oils of *Eugenia uniflora* leaves has been confirmed by evaluating the samples collecting from different seasons. The sample collected during dry seasons (April-september) contains high percentage of spathulenol and caryophyllene oxide (important constituents in the oil) [8]. This result may be correlated with the biotic pressures which could modulate sample volatiles.

The effect of seasonal variation on genotypes of Mentha species was assessed for essential oil content. *Mentha canadensis* had shown the highest menthol content (5.3% in February and lowest in May (3.5%) [9]. It has been demonstrated that genetic expression for oil production is also affected by plant ontogeny and environmental regulation, seasonal variations [10, 11]. The environmental conditions of temperature and precipitation, probably affected the volatile oil content. In February, the average temperature was 6.9ºC higher with a long-day photoperiod of 14 hours, increasing carbon assimilation and biomass production.

In another study, the seasonal variation of the essential oil composition of *Origanum syriacum* was assessed. Thymol, the main component of the oil was found highest in summer (46.70%). But the other chemical p-cymene found in highest amount in early spring (62.18%) [12]. According to Marotti et al[13], long photoperiods increased the content of essential oils in the foliage and of phenolic monoterpenes in the oil [14].

The volatile oil of matured leaves in *Eucalyptus* species were determined in different seasons varied from 0.05% during winter to 2.5% during summer season. Best essential oils percentages were estimated in *E. camaldulensis* and *E. cinerea* (2.5 and 1.95% respectively) in the summer season. This may be due to the physical and chemical stress on plant especially during summer drought. This stress led to plant secretion to different defense components called secondary metabolites, as protecting agents, especially terpenoid compounds (essential oils). These results are in agreement with the results obtained by Samuelsson (1999) [15].

In contrast the essential oils from the aerial parts of basil (*Ocimum basilicum*) showed the maximum amounts of essential oil in winter and minimum in summer. This low essential oil yields in summer might be attributed to high temperature and partial evaporation of some constituents of oil [16].

Effect of seasonal variation on nonvolatile secondary metabolite content

A study carried out on total phenolic content in *Camellia sinensis* during three harvest time (May, July, September). The content of total phenolics increased in July (80.69 µg/mg), followed by September (62.88µg/mg) and decreased in May (59.44 µg/mg) [35]. Harbowy & Balentine describes biosynthesis of phenolic compounds can be effectively induced by sunlight. That is why in shaded tea flushes the concentrations of total phenolics are much lower. On the basis of this information, the differences in total phenolic levels between fresh leaves harvested in cooler (May and September) and warmer months (July) in Turkey may not be a temperature effect but also a day length and sunlight effect [36].

TABLE 1: EFFECT OF SEASONAL VARIATION ON VOLATILE CONTENTS OF SOME IMPORTANT MEDICINAL PLANTS

S.no.	Medicinal plant	Content evaluated	Season optimised
1.	*Achillea filipendulina* (Asteraceae)	% yield of volatile oil	Summer [17]
2.	*Artemisia annua* (Asteraceae)	% yield of volatile oil in sand loamy soil and clay loamy soil	Autumn-Summer [18]
3.	*Cistus monspeliensi* (Cistaceae)	% yield of essential oil	Spring [19]
4.	*Clinopodium pulegium (Lamiaceae)*	% yield of essential oil	Summer [20]
5.	*Eucalyptus citriodora* (Myrtaceae)	citronellal citronellol citronellyl acetate	Autumn [21] Winter Spring
6.	*Lauris nobilis (Lauraceae)*	% yield of extract	Summer [22]
7.	*Mentha longifolia* *Mentha arvensis* *Mentha piperata* (Lamiaceae)	% yield of volatile oil	Summer [23]
8.	*Micrmeria fruticosa (Lamiaceae)*	limonene, menthone, menthol	Summer- Spring [24]
9.	*Ocimum gratissimum* (Lamiaceae)	% yield of volatile oil	Spring [25]
10.	*Origanum cyrenaicum* (Labiatae)	monoterpenes hydrocarbon oxygenated sesquiterpene hydrocarbon	Spring [26] Spring
11.	*Pelargonium graveolens* (Geraniaceae)	% yield of volatile oil geranium	Summer [27] Winter
12.	*Pistacia atlantica* (Anacardiaceae)	% yield of volatile oil	Spring [28]
13.	*Plectranthus amboinicus* (Lamiaceae)	% yield of essential oil	Spring [29]
14.	*Santolina chamecyparissus* (Asteraceae)	limonene, pinene, caryophylline oxide	Summer [30]
15.	*Sclerocerya birrea* (Anacardiaceae)	% yield of volatile oil	August [31]
16.	*Thymbra spicata* *Saturejathymbra* *Salvia fruticosa* *Menthapulegium* (Labiatae)	% yield of volatile oil	Summer [32]
17.	*Thymus vulgaris* (Lamiaceae)	% yield of volatile oil	Winter [33]
18.	*Valeriana jatamansi* (Caprifoliaceae)	% yield of volatile oil	Autumn-Summer [34]

Deshmukh and Dhunal have been noticed the effect of seasonal variation on secondary metabolites in *Sorghum bicolor* in four promising cultivars of sorghum (RSV-669, RSV-626, RSV-623, RSV-629, RSLG-262. Reducing sugars, proline, glycine betaine and free amino acids had been increased with increasing water stress. On the basis of this, the promising cultivars RSV-669 and RSV-629 can be designated as drought tolerant and the cultivar RSV-626 as moderate drought tolerant, while the cultivar RSV-623 can be considered as drought susceptible. Based on the results it has been considered that phenolic content increased under= water stress by hydrolyzing the glycosides [37]. There is a hypothesis that water stress can stimulate the accumulation of phenolic compounds. Kavi Kishore et al explains the dramatic accumulation of proline due to increased synthesis and decreased degradation under a variety of stress conditions was due to both regulations of proline biosynthetic pathway enzymes and up regulation of proline degrading enzymes [38].

St. John's Wort (*Hypericum perforatum*), was harvested in different seasons for the optimization collection of aerial parts of two varieties (broad leaf biotype and narrow leaf biotype) of the plant with respect to hypericin and pseudohypericin (bioactive constituents). In a broad leaf biotype, the hypericin and pseudohypericin concentration varied from a winter minimum of less than 100 ppm to a summer maximum approaching 3000 ppm and in the narrow leaf biotype increased from similar winter values to summer maxima approaching 5000 ppm [39].

The contents of Bacoside-A (*Bacopa monneiri*) was found highest in July-October (Monsoon period) and lowest was found in March-June (Summer). These results might be due to high humidity, temperature and availability of large amount of water during monsoon period which are favourable conditions for the growth of *B. monnieri* plants [40].

The shoots of *Mentha longifolia*, collected during different seasons from a natural habitat were evaluated for alkaloid, flavonoid and phenolic contents. The study concluded that the winter is the best season for polyphenol and flavonoid content followed by summer and then autumn season.[41] During winter, most of the herbs complete their life cycle and start drying up. As fats and proteins are the end products of metabolic reactions in drying shoots, they are naturally higher at this stage. Those results in maximum energy during the winter season [42]. The higher concentration of phenolics and flavonoids during winter may have been due to low temperature stress as well as maturity of the plants [43]. During Winter, higher alkaloids might indicate some sort of nutritional stress in this season or a complex interaction between soil and environment.

In another study, variation in chemical profile and phenolic content in *Glycyrriza glabra* from plant harvesting in month of February to November. The major constituents liquiritin and glycyrrhizin were highest in February whereas glabridin and glabrene were found highest in November. The total phenolic content was found highest in November [44]. Phenolic compounds increases with increasing light intensity [45]. The lower contents of phenolic compounds in February could be due to decreased active biosynthesis during cooler weather, as was previously remarked [46].

Total polyphenols and flavonoid contents were determined in the leaves of *Chelidonium majus* L. during different seasons. The highest concentration of total phenolic compounds were obtained from plants collected during the spring when the plant is in the rosette stage (60.96 mg GA/g). The highest concentration of flavonoids (291.58 mg RU/g) was recorded during the month of autumn, just before flowering. At the beginning of the flowering stage, there is a lack of that concentration, which again increases when the plant begins with the formation of fruit [47]. Moreover, the results of other studies carried out to evaluate the seasonal variation in tabulated form (**Table 2**).

TABLE 2: THE EFFECT OF SEASONAL VARIATION ON THE NON-VOLATILE COMPONENTS OF POPULAR MEDICINAL PLANTS.

S. No.	Name of plant	Content determined	Season optimised
1.	*Adhatoda vasica* (Acanthaceae)	vasicine deoxyvasicine	Rainy [48] Winter
2.	*Apis mellifera* (Apidae)	phenolic	Winter [49]
3.	*Catharanthus roseus* (Apocynaceae)	flavonoids	Winter [50] Summer
	Ocimum sanctum (Lamiaceae)		Rainy
4.	*Convolvulus microphyllus (Convolvulaceae)*	chlorophyll, proline, alkaloids and phenols	Summer [51]
	Datura metel (Solanaceae)		Rainy Season
	Withania somnifera (Solanaceae)		Winter
5.	*Ipomoea pes-Caprae* (Convolvulaceae)	total phenolic content flavonoids	Summer-Spring [52] Winter
6.	*Mellitus melissophyllum* (Lamiaceae)	flavonoid	Spring [53]

7.	Parkia biglobosa (Mimisaceae)	flavonoids	Spring [54]
8.	*Phyllanthus amarus (Lamiaceae)*	total alkaloids flavonoids	Summer [55]
9.	*Prunus amygdalus* (Rosaceae)	total phenolic content for stems leaves	Summer [56] Spring
10.	*Pseudobombax marginatum* (Bombacaceae)	total polyphenols flavonoids	Winter [57] Summer
	Guapira graciliflora (Nyctaginaceae)	total polyphenols flavonoids	Summer Winter

Effect of seasonal variation on biological activities:

Plethora of reports available, claims the significant effect of seasonal variation on the pharmacological activities of the medicinal plants., Seasonal variation was found to influenced the antidiabetic activity of *Momordica charantia* fruits. The highest value of antidiabetic activity was found in spring season, followed by summer, autumn and winter season (66±2%) [58]. This variation in the results may be attributed to the difference in quantity or quality of the active compounds in the fruits. As different seasons of the year could directly or indirectly affect the availability of some precursors that the plant needs for the biosynthesis of the active ingredients [59].

Antioxidant activity and active compounds content from the flowers of *Bellis perennis* was investigated. The most significant activity was observed in the flower sample collected from spring to autumn seasons because the changes of determined metabolites and antioxidant activity in daisy flowers seem to be brought about by immediate fluctuations in environmental factors, such as day and night temperatures, rainfalls, drought, and the duration and intensity of sunshine [60].

In another study, Influence of seasonal variation on antioxidant activity of *Ocimum basilicum* extract was evaluated. The winter seasons sample shown the best antioxidant activity with IC_{50} value 4.8 μg/ml [16].

In another study, seasonal discrepancy in antioxidant potential from bark of *Nothapodytes nimmoniana* was investigated. DPPH and FRAP antioxidant assays were found highest during the month of winter (December). The physiological and biochemical changes are synergistic effects of different biotic and abiotic parameters. In most of the plants exposure to high or low temperature than the optimum is regarded to be the main cause suggesting temperature to be the regulating factor. Low rate of dehydration due to low temperature and high rainfall forms to be the probable reason for this drop [61].

In another study, effect of seasonal variation on antioxidant activity of *Ginkgo biloba* was investigated. Antioxidant activity was performed by three assays i.e. DPPH, FRAP and ABTS. In ABTS and DPPH Assays, antioxidant activity was highest in autumn and In ABTS, highest value was found in spring. Antioxidant activity is correlated with phenolic content. Variation in phytochemicals arise due to specific environmental conditions including biotic and abiotic factors. With increase in altitude, environmental conditions such as UV radiation, temperature, rainfall, moisture etc. changes occur rapidly. The locations falling between 1742 and 2260m altitude representing temperature climatic condition, are likely to be associated with higher contents of phytochemicals and antioxidant. Findings on production of polyphenols and antioxidant, in respect to environmental stress, have been linked to defense mechanism [62].

In this study, effect of seasonal variation on antioxidant and gastroprotective activities of licorice extracts (LE) were investigated. The samples from May and November showed the most favorable free radical scavenging and antioxidant effects, whereas the best gastroprotective effect was in May. Liquiritin and glycyrrhizin, the major constituents in the February and May (LE), appeared to contribute to the superoxide radical scavenging and gastroprotective effects. Glabridin and glabrene, the compounds with the highest relative proportion in the November (LE), accounted for the antioxidant and DPPH scavenging activities of licorice. It is concluded that the chemical profile of licorice quantitatively varied at different harvest times and these fluctuations determined changes in its bioactivities [44]. Moreover, results of several other research works are presented in the tabular form (**Table 3**).

TABLE 3: THE EFFECT OF SEASONAL VARIATION ON THE PHARMACOLOGICAL ACTIVITIES OF SOME MEDICINAL PLANTS.

S.No.	Name of plant	Activity determined	Season Optimised
1.	*Alstonia scholaris* (Apocynaceae)	Antineoplastic	Summer [63]
2.	*Athrixia phylicoides* (Asteraceae)	Antioxidant	Winter [64] and Summer
3.	*Baccharis dentate* (Asteraceae)	Antioxidant	Summer [65] and Winter
4.	*Combretum roxburghii* (Combretaceae)	Antioxidant	Winter [66] and spring
5.	*Melilotus indicus* (Fabaceae)	Antioxidant activity of methanolic and chloroform fraction	Autumn [67]
6.	*Myrtus communis* (Myrtaceae)	Antioxidant	Rainy [68]
7.	*Pistacia lentiscus* (Anacardiaceae)	Antioxidant	Autumn [68]
8.	*Porcelia macrocarpa* (Annonaceae)	Antimicrobial	Winter [69]
9.	*Rhoicissus tridentate* (Vitaceae)	Uterotonic	Summer [70] and Autumn
10.	*Rosmarinus officinalis* (Lamiaceae)	Antioxidant activity of carnosic acid	Winter [71]
11.	*Salvia sclarea* (Lamiaceae)	Antioxidant	Summer [72]
12.	*Tulbaghia violacea* (Alliaceae) *Hypoxis hemerocallidea* (Hypoxidaceae) *Drimia robusta* (Hycinthaceae) *Merwilla plumbea* (Hyacinthaceae)	Antibacterial	Winter [73] and Autumn
13.	*Zizyphus spina christi*	Antihyperglycaemic activity	Summer [74]

CONCLUSION: The current review revealed that there is no generalities should be considered while harvesting the parts of the plants. As the activity of medicinal plants are depends upon the chemical constituents present in them. Variation in the amount may results in loss of activity which can make the researcher to draw the false/wrong perception about the efficacy of the plants with potent traditional value drug. The plants especially perennial herbs should be first evaluated for their optimum season of harvesting with respect to their constituents of commercial and/or pharmaceutical significance.

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