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Methyl-jasmonate and salicylic acid as potent elicitors for secondary metabolite production in medicinal plants: A review

Ankita Singh and Padmanabh Dwivedi

Abstract
Secondary metabolites are the bioactive compounds of plants which have no role in the development process but are needed for defense purposes. Their synthesis takes place from the primary metabolism of the plant. Plants are a novel source of bioactive compounds from which different drugs are derived. These bioactive compounds have therapeutic value for which they are used all over the world. As medicinal plants are used for the extraction of different compounds they are exploited and becoming threatened. To overcome this problem and to preserve the resulting loss of biodiversity we can conserve the medicinal plants by propagation and the production of secondary metabolites by different *in vitro* culture techniques. As we know that intact plant has a low potential for chemical synthesis of bioactive compounds so to enhance the production of secondary metabolites elicitors are used. Elicitors are those molecules which enhance the secondary metabolism of the plant. Elicitors may be biotic or abiotic. The present review deals with the synthesis and enhancement of different bioactive compounds by Methyl-Jasmonate (MeJA), Jasmonate (JA) and Salicylic Acid (SA) as elicitors of many medicinal plants *in vitro* by using different cultures.

Keywords: Elicitors, *in vitro*, medicinal plants, methyl-jasmonate and salicylic acid, secondary metabolites.

Introduction
Secondary metabolites are the biologically active compounds which are synthesized during primary metabolism of plants, they do not have any developmental role in plants but are needed in plant defense against herbivore and pathogen also confer protection against environmental stresses. Secondary metabolites are used as pharmaceuticals, agrochemicals aromatics, food additives (Oksman-Caldentey *et al*., 2004) [54]. Secondary metabolites or phytopharmaceuticals include alkaloids, glycosides, phenols, flavonoids, volatile oils, etc. There are three major groups of secondary metabolites viz terpenes, phenolics, and Nitrogen and Sulphur containing compounds. Medicinal plants are the source of bioactive compounds with many blockbuster drugs derived directly or indirectly from plants having therapeutic value. The drugs which are derived from the plants are used globally. It has been reported by WHO that 80% of the world's population rely on medicinal plants for their primary health (Raskin *et al*., 2002) [62]. The production of secondary metabolites in plants is often low (less than 1% dry weight) and depends greatly on the physiological and developmental stage of the plant (Rao *et al*., 2002; Thakur *et al*., 2013) [67, 76]. The medicinal plants are used world wide for curing purposes; they are so in demand that they gain pharmaceutical importance by which the medicinal plants are exploited at a higher rate and most of them are threatened. To overcome this problem we can preserve the resulting loss of biodiversity by minimising use of the product from the intact plant and synthesize secondary metabolite production using *in vitro* techniques by elicitors for enhancing their bio-production to meet commercial demands. Plant tissue culture is a novel approach for the large-scale bio-production of valuable secondary products. Plant tissue culture techniques use plant cells, tissues and organs cultivated under an aseptic condition which is independent of abiotic factors for producing metabolites. Secondary metabolites are extracted from the medicinal plants having herbal and pharmaceutical importance on a commercial scale.

Elicitors
Molecules that stimulate secondary metabolism are called as "elicitors." Elicitors may be biotic or abiotic. "Elicitation" is a process of inducing or enhancing synthesis of a secondary metabolite by the plants to ensure their survival, persistence, and competitiveness (Namdeo 2007) [51]. Elicitation has been widely used to increase the production or to induce *de novo*

synthesis of secondary metabolite in *in vitro* plant cell culture (Dicosmo *et al*., 1985) [14]. This opened up a new area of research that could have important economic benefits for the pharmaceuticals industry. Several parameters such as elicitor concentration, and selectivity, duration of elicitor exposure, the age of culture, cell line, growth regulation, nutrient composition and quality of cell wall materials are some of the important factors influencing the successful production of secondary metabolite (Ganapathi *et al*., 1990) [26]. Phytohormone elicitors used in elicitation studies are Methyl-Jasmonate (MeJA) and Salicylic acid (SA) because of their key roles in enhancing biologically active compounds of pharmaceuticals importance.

Methyl-Jasmonate (MeJA) and Jasmonic acid (JA)

Methyl-jasmonate and Jasmonic acid are produced widely in plants, notably as a 'stress hormone', a response to attack by insects, which deters feeding. Being volatile, it can also signal, such attack to neighboring undamaged plants, which may increase production of jasmonates. In 1962, MeJa was primarily isolated from the essential oil of *Jasminum grandifloram.* Jasmonic acid (JA) and its methyl ester, methyl jasmonate (MeJA), have been proposed to be important signaling compounds in the process of elicitation leading to the hyperproduction of various secondary metabolites (Walker *et al*., 2002) [80]. They have also been reported to play a key role in signal transduction processes that regulate defense responses in plants and shown effectiveness to enhance the production of secondary metabolites in cell cultures (Zhao *et al*., 2010). Jasmonates are plant-specific signaling molecules that activate several important and physiological and developmental processes (Farmer *et al*., 2005). Methyl jasmonate help in inhibiting the proliferation of two types of human prostrate cancer cell *in vitro* (Samaila *et al*., 2004) [70]. It similarly suppressed the cell proliferation in human breast, melanoma and lymphoblastic leukemia cells (Fingrut and Flescher 2002) [19]. A characteristic of jasmonates is that they selectively kill cancer cells while sparing normal cells (Flescher 2005). Several *in vitro* studies showing cytotoxic effects of methyl-jasmonate are cited in a review of Cohen and Flescher (2009) [13].

Salicylic acid (SA)

Salicylic acid, well known for systemic acquired resistance, induces in the plant response to many pathogens, can also elicit the production of secondary metabolites in plants (Hayat *et al*., 2010; Pieterse *et al*., 1999) [31, 59].

In this review we have focused mainly on the action of the commonly use Methyl Jasmonate (MeJA), Jasmonate and Salicylic acid (SA) effect on different medicinal plants to enhance the biosynthesis and accumulation of secondary metabolite production of pharmaceutical importance.

Medicinal plants of pharmaceutical interest whose secondary metabolite production is enhanced by the addition of Methyl-Jasmonate (MeJA), Jasmonate and Salicylic acid (SA)

Artemisia absinthium is a herbaceous perennial plant with fibrous roots belong to the Asteraceae family and commonly called as wormwood. It is gaining resurgence due to its extensive pharmacological activities like antimalarial, anticancer and antioxidant. Artemisinin is the major metabolite for antimalarial effects. Flavonoids and terpenoids used synergistically to boost the bioavailability of artemisinin. However, due to limited quantities of this metabolite in wild plants, *in vitro* cultures were established, and strategies have been adopted to enhance the metabolites in the culture (Ali *et al*., 2015) [4]. Methyl Jasmonate (MeJA) and Jasmonic Acid (JA) together as an elicitor with a phytohormone Gibberellic acid (GA) used to increase the accumulation of secondary metabolite, i.e., artemisinin in cell suspension culture of *A. absinthium* (Ali *et al*., 2015) [4].

Ajuga bracteosa is an endangered medicinal hairy herb belong to the Lamiaceae family and commonly called as Nilkanthi in Sanskrit. It is used globally to cure many serious ailments like gout, rheumatism, palsy and amenorrhoea (Anonymous, 1985). It is effectively used for jaundice, hypertension, sore throat and as a blood purifier (Hamayun *et al*., 2006) [32]. Investigators have been reported antimalarial activities (Njorge *et al*., 2006) [52]. Phytoecdysteroids is one of the major compound synthesized by *A. bracteosa* and is structural analogs of the insect molting hormone ecdysone. In plants, these compound are responsible for some physiological functions. Hairy roots are valuable biotechnological tool for the production of secondary metabolites due to their high productivity (Pistelli *et al*., 2010) [58]. Phytoecdysteroids levels were enhanced by 14 days of MeJA elicitation in *A. bracteosa* (Khan *et al*., 2017) [73]. Methyl jasmonate (MeJA) and phenyl acetic acid (PAA) together used as elicitors which induced enhancement in phenolic content (total phenolic content) and flavonoid content (total flavonoid content) in root suspension of *A. bracteosa* (Saeed *et al*., 2017) [73].

Bacopa monnieri is a perennial creeping herb and belong to the Scrophulariaceae family. It is commonly known as water hyssop, Indian pennywort and also known as "Brahmi" in Ayurveda. It is nootropic herb that has been used in traditional medicine for longevity and cognitive enhancement. Supplementation can reduce anxiety and improve memory formation. Bacosides are triterpenoids saponins. Bacoside A is considered as major active component known to have protective activities against morphine-induced cerebral toxicity, chemical-induced liver toxicity and wound healing activity (Russo *et al*., 2005) [68]. The production bioactive compound Bacoside A was enhanced by using MeJA as an elicitor *in vitro* shoot culture of *B. Monneiri* (Sharma *et al*., 2013) [69, 76].

Catharanthus roseus is a perennial herb which belong to the Apocynaceae family and commonly known as Periwinkles. Its therapeutic benefit is due to the presence of terpenoid indole alkaloids, such as antihypertensive, ajmalicine and serpentine; and antitumoural alkaloids; vincristine and vinblastine, which have been used in chemotherapy, since 1960's (Heiden *et al*., 2004; Feranandez *et al*., 2013) [18]. The total indole alkaloids biosynthesis is extremely low, to increase this production, several approaches were tried (Zhao *et al*., 2007) using *C. roseus* cell culture, being genetic modification or modification or metabolic engineering the most promising biotechnological alternatives for producing these compounds (Heijden *et al*., 2004) [77, 79]. It was reported that MeJA and β-cyclodextrin (β-CD) in combination increased the production of bioactive alkaloids in cambial meristematic cells (CMCs) of C. Roseus (Zhou *et al*., 2015) [57]. The joint use of MeJA and cyclodextrins, when accompanied by a short exposure to UV, enhanced the extracellular ajmalicine accumulation in suspension cultured cells in *C. roseus*. Here, the use of cyclodextrins not only induced ajmalicine biosynthesis but also promote adduct formation (Almagro *et al*., 2011) [5].

Gymnemic sylvestre is an important medicinal climber belong to the Asclepiadaceae. This climber is extensively used in

almost all the Indian systems of medicine as a remedy for rheumatism, cough, ulcer, and pain in the eyes. It is useful for inflammations, dyspepsia, constipation, jaundice, and so forth. The roots of this plant have been reported as a remedy for snakebite (Nadkarni 1993) [53]. *G. Sylvestre* is an important diabetic medicinal plant which yields pharmaceutically active compounds called gymnemic acid (GA), which is a group of closely related triterpenoid saponins. MeJA reported yielding the maximum gymnemic acid content in a cell suspension culture. Similarly, Salicylic acid also tested as an elicitor in cell suspension culture of *G. sylvestre* to enhance the gymnemic acid, but SA evoked a moderate response (Bhuvneshwari *et al*., 2015).

Hypericum perforatum is a sprawling, leafy herb and belong to the Hyperaceae family. It is a well known medicinal plant commonly called as St. John's wort or Perforate St. John's wort with antidepressant activity and anti-inflammatory properties (Wolfle *et al*., 2014; Gartlehner *et al*., 2015) [25]. The main pharmacological properties are due to the presence of naphtodianthrones such as hyperian and pseudohypericin. The production of hypericin and pseudohyperian has doubled in the elicited cell suspension culture of salicylic acid (Gadzovska *et al*., 2013) [22].

Panax ginseng is a perennial herb of the Araliaceae family, is well known traditional medicine plant and its root has been used as a herbal remedy for various disorders (Akerele 1992) [3] The herb is of pharmacological importance because of the presence of major bioactive compound triterpene saponin called Ginsenoside (Rahimi *et al*., 2015) [64]. Ginsenoside Rg3 is not naturally produced in ginseng. To determine whether Rg3 is synthesized in gingseng, hairy root treated with methyl-jasmonate (MeJA) and it was found that Rg3 did accumulate in hairy roots that were MeJA-treated for 7 days (Kim *et al*., 2013) [45]. Adventitious roots of ginseng were treated with MeJA up to 150µM and cultured for 40 days, up to 100µM MeJA inhibited the root growth but increase the ginsenoside accumulation (Kim *et al*., 2004) [44].

Plumbago indica is an evergreen shrub which belong to Plumbaginaceae family and commonly called as Indian leadwort, Scarlet leadwort or whorled plantain. Plumbagin is a naphthoquinone isolated from the roots of *Plumbago* species is well known for diverse pharmacological properties. Plumbagin has been shown to exert anticancer and anti-proliferative activities in animal models and cell culture (Sandur *et al*., 2006). Plumbagin also induces apoptosis in human PCa cell lines (Powolny *et al*., 2008) [61]. *In vitro* root cultures with salicylic acid and naphthalene (N) were established to enhance the extracellular excretion of plumbagin in *P. indica* (Jaisi and Panichayupkaranant 2014). It has been reported that elicitation by Jasmonic acid (JA) in hairy root culture of *P. indica* enhanced the production of its bioactive compound plumbagin (Gangopadhayay *et al*., 2011) [23]. *Portulaca oleracea* is an annual succulent in the Portulacaceae family. Its common name is purslane, verdolaga, little hogweed, red root. Dopamine had a stimulatory effect on the various nervous system and used for treatment of Parkinson's disease, congestive heart failure, and myocardial dysfunction (Dighe *et al*., 2008) [15]. MeJA and SA both used as an elicitors to test whether they stimulate dopamine in hairy root culture of *Portulaca* and it was reported that MeJA have a high stimulatory effect on the production of dopamine in *Portulaca* hairy roots while SA not proved to be an appropriate elicitor to increase dopamine in *Portulaca* hairy roots (Moghadham *et al*., 2013).

Podophyllum hexandrum is an endangered medicinal herb and belong to the Berberidaceae family. Its common name is May apple, American mendlake. May apple has been used by American Indians as an emetic, cathartic (Ernest *et al*., 1999) [16] and antihelmintic agent (Ernest *et al*., 1999) [16]. It is a principle source of podophyllotoxin (ptox). Ptox is a polyphenolic substance, a precursor to semi-synthetic anticancer drugs (Gordaliza *et al*., 2004) [28]. Mechanism action of ptox is based on inhibiting the polymerization of tubulin and arresting the cell cycle in the metaphase (Ayres and Loike 1990, Buss and Waigh 1995) [6, 10]. MeJA induced ROS production, which stimulated ptox accumulation and upregulated three ROS- responsive ptox biosynthetic gene, namely PhCAD3, PhCAD4 (Cinnamyl alcohol dehydrogenase) and by increasing their mRNA stability (Saptarshi *et al*., 2017) [71].

Salvia miltiorrhiza is a deciduous perennial plant; well-known traditional Chinese medicinal herb belong to the Labiatae family. It is commonly called a Red sage. It has been used for the treatment of cardiovascular disease, microcirculation disorders, liver fibrosis, cancer, insomania, poor memory and mental agitation. The fat-soluble components are diterpene compounds belonging to the subclass ‘tanshinones' (Zhou *et al*., 2005) [57]. The importance of this plant is due to the presence of the bioactive compound tanshinones with notable pharmacological activities. Plant tissue culture is the major biotechnological processes for the rapid production of tanshinones in the herb. Various *in vitro* cultures of *S. miltiorrhiza* has been established, including cell suspension culture, adventitious root, and hairy root cultures, which can accumulate the major tanshinones as in the plant's roots. Tanshinones production in cell and hairy root cultures has been dramatically enhanced with various strategies, including medium optimization, elicitor stimulation and nutrient feeding operation (Wang *et al*., 2010) [81]. It has been reported that MeJA with transgenic technology in hairy root culture highly enhanced the production of tanshinones in *S. miltiorrhiza* (Hao *et al*., 2015) [30].

Satureja khuzistanica may be annual or perennial belong to the Lamiaceae family, and it is commonly known as Savory. It used traditional Iranian medicine, and now it is an endemic plant of Iran and widely distributed in the southern part of the country (Jamzad., *et al*., 1996, Vosough-Ghanbari *et al*., 2010) [37, 78]. Rosmarinic possesses various biological activities, such as antimicrobial, anti-mutagenic, antioxidant and treatment of slowing the development of Alzheimer, cancer chemoprotection and anti-inflammatory activity (Petersen and Simmonds 2003) [56]; Bulgakov *et al*., 2012) [9]. Rosmarinic acid (RA) is a common water-soluble phenolic compound (Khojasteh *et al*., 2014; Georgiev and Weber 2014) [39. 24]. RA, derived from a caffeic acid and 3,4-dihydroxy phenyllactic acid (Peterson *et al*., 2003). RA used as an interesting product in both pharmaceuticals and cosmetic industries. As the demand for the bioactive product grows, it is needed to increase the extraction of metabolites from limited natural plant resources. For improving production of rosmarinic acid, MeJA is used as an elicitor in cell suspension culture of *S. khuzistanica* (Abbas *et al*., 2016).

Stephania venosa is a herbaceous perennial vine belongs to the family Menispermaceae and is an indigenous medicinal herb. It is commonly known as blood soap. The prominent red sap in its stem is a characteristic key for the species identification used as a tonic drug, for the treatment of cancer and diabetes, aphrodisiac (Ingkaninan *et al*., 2006). Dicentrine, a known alpha 1- adrenoceptor antagonist, could

have a therapeutic potential to develop as antihypersensitive, antihyperlipidemic and other cardiovascular drugs (Jai *et al*., 1994; Yu *et al*., 1994) [36, 84]. It has been reported that salicylic acid (SA) and Chitosan in combination increased the bioactive compound dicentrine in cell suspension culture (Kitisripanya *et al*., 2013) [46].

Silybum marianum is an annual or biennial plant of the Asteraceae family. Its common name includes Milk thistle. Its medicinal importance may appear to stimulate pro-lactation due to possible estrogenic activity (Foong *et al*., 2015) [21]. Also used in for a number of purposes including treatment of liver disease, prevention and treatment of cancer, and supporting of poisoning of death cup mushroom; however clinical study and results were described as heterogenous and contradictory (Rainone and Francine 2005) [66]. Silymarin is a mixture of flavono lignans extracted from *S. marianum*. The main component of silymarin is silibinin, silydianin, and silychristin and taxifolin (Ferenci *et al*., 2016) [17]. It has been reported that bioactive compound of *S. marianum* in cell suspension culture is increased when it was elicited by the MeJA and methyl B cyclodextrin (Corchete *et al*., 2013) [12].

Taxus bacata is a small coniferous trees or shrubs in the yew family of Taxaceae. Its common name is Yew. Taxus was the initial sources of paclitaxel or Taxol, a chemotherapeutic drug used in breast and lung cancer treatment and, more recently in the production of the Taxus drug eluting stent by Boston Scientific. Over-harvesting of the yew for paclitaxel led to fear that it would become an endangered species, the drug was harvested from the bark of the yew, the harvesting of which kills the tree in the processes (Gersmann and Hannna 2010; Aldred and Jessica 2011) [27]. Taxanes are a class of anticancer agents that bind to and stabilize microtubules causing cell-cycle arrest and apoptosis (cell death). Plant cell culture is used for the industrial-scale biotechnological production of important bioactive secondary metabolite including the anticancer, paclitaxel (Onrubia *et al*., 2013) [55]. Bio-processing of plant *in vitro* system for the mass production of pharmaceutically important metabolites: Paclitaxel and its derivatives. It is reported that addition of MeJA to cell culture is currently most important strategies for increasing taxane yields, because its exogenous application enhances secondary metabolite production in a variety of plant species, including Taxus species (Bentebibel *et al*., 2005; Ketchum *et al.*, 1999; Yukimune *et al*., 1996) [7, 42, 83]. Similarly, cyclodextrins (CD's) have also attracted considerable attention as agents capable of inducing a defense response in plant cell culture and therefore acting as true elicitor (Bru *et al*., 2006; Lijavetzsky *et al*., 2008; Zamboni *et al*., 2009) [8, 47, 86]. The Taxol biosynthesis can be increased by the joint action of MeJA and cyclodextrins, reaching production levels 55 times higher than in non-elicited cultures (Sabataer-Jara *et al*., 2014) [72]. Similarly, MeJA and Squalestatin (S) are effective elicitors for increasing phenolic production in cell suspension culture, likely through increasing LOX activity followed by an increased in endogenous jasmonate (Pour *et al*., 2014) [60].

Thevetia peruviana is a small tree which belongs to the family Apocyanaceae. Its common name is Mexican oleander, yellow oleander, luckynut tree. It produces several compounds with the pharmaceutical application, among which peruvoside could be highlighted. However, the compound produced in low concentration in the plant, to obtain the higher quantities of the desired product used MeJA as elicitors. Peruviside is used in the treatment of mild cardiac suffering and a weak heart (Neelam Rajbhar and Anil Kumar 2014). Pharmacological importance are due to its anti-inflammatory, antimicrobial, anti-termite anti-fungal properties, anti-spermatogenic properties (Neelam Rajbhar and Anil Kumar 2014). The elicitor MeJa in cell suspension culture in Schenk-Hidebrant (SH) medium enhanced *in vitro* peruviside production in *T. peruviana* (Zabala *et al*., 2010) [85, 48].

Withania somnifera is a perennial ayurvedic herb belong to the Solanaceae family and commonly known as Ashwagandha, Indian gingseng. The biologically active chemical constituents are steroidal lactones withanolides, withaferins and withanoloides. Withanolides are steroidal and bear a resemblance, both in their action and appearance, to the active constituents of Asian gingseng (Panax gingseng) known as ginsenosides. The plant is in demand always due to its pharmacological value as an adaptogen, antibiotic, aboritifacient, aphrosidiac, astringent, anti-inflammatory, deoobstruent, diuretic, narcotic, sedative, and tonic (Abhou-Douh 2002) [1]. It has been reported that hairy root culture of *W. somnifera*, when elicitated by MeJA, enhanced the production of the bioactive compounds Withanolide A, Withanone, Withaferin A (Sivanandhan *et al*., 2012) [74]

Conclusion

The present review reports the information about the use of Methyl-jasmonate (MeJA) and Salicylic acid (SA) as elicitors in medicinal plants for the enhancement of their bioactive compounds by different *in vitro* culture techniques to meet the commercial demands of pharmaceuticals. It is found that medicinal plants are used across the globe to cure various diseases like malaria, jaundice, hypertension, tumor, depression, constipation, dyspepsia, rheumatism, cancer, diabetes, etc. These plants have medicinal properties due to presence of a bioactive compound in them. The bioactive compound in the intact plant is less in quantity so to synthesize secondary metabolites in desired quantity, Methyl-Jasmonate (MeJA), and Salicylic acid (SA) are used as elicitors *in vitro* using different cultures.

Table 1: Effect of Methyl-Jasmonate (MeJA) and Salicylic Acid (SA) as elicitors on secondary metabolites production of medicinal plants *in vitro* culture.

S. No.	Plant species	Elicitors	Secondary Metabolites	Type of culture	Reference (s)
1.	*Artemesia absinthium*	MeJA, JA and GA	TPC and TFC	Suspension	Ali *et al*., 2015
2.	*Ajuga bracteosa*	MeJA and PAA	TPC and TFC	Root suspension	Saeed *et al*., 2017
3.	*Ajuga bracteosa*	MeJA	Phytoecydysteroids	Hairy root	Khan *et al*., 2017
4.	*Bacopa monnieri*	MeJA	Bacoside A	Shoot	Sharma *et al*., 2013
5.	*Catharanthus roseus*	MeJA and Cyclodextrin	Ajmalicine	Cell	Ajmagro *et al*., 2011
6.	*Catharanthus roseus*	MeJA and Cyclodextrin	Ajmalicine	Cambial meristematic cells	Zhou *et al*., 2015
7.	*Centella asiatica*	MeJA and Yeast	Asiaticoside	Whole plant	Kim *et al*., 2004
8.	*Centella asiatica*	MeJA	Asiaticoside	Hairy root	Kim *et al*., 2007

9.	*Centella asiatica*	MeJA	Centelloside	Cell suspension	Mercedes *et al*., 2011
10.	*Gymnema sylvestre*	MeJA	Gymnemic acid	Cell suspension	Chodisetti *et al*., 2015
11.	*Hypercium perforatum*	MeJA	Flavonoid (Hyperin and Quercetin)	Cell suspension	Wang *et al*., 2015
12.	*Hypericum perforatum*	SA	Hypericin and pseudo hypericin	Cell suspension	Gadzovska *et al*., 2013
13.	*Panax gingseng*	MeJA	Ginsenosides	Hairy root lines	Corchete *et al*., 2013
14.	*Panax gingseng*	MeJA	Gingsenosides (Rg 3)		Kim *et al*., 2004
15.	*Plumbago indica*	JA	Plumbagin	Hairy root	Gangopadhyay *et al*., 2011
16.	*Portulaca oleracea*	MeJaA and SA	Dopamine	Hairy root	Ahmadi *et al*., 2013
17.	*Podophyllum hexandrum*	MeJA	Podophylloxin (ptox)	Cell	Hazra *et al*., 2017
18.	*Salvia miltiorrhiza*	MeJA	Tashinones	Hairy root	Hao *et al*., 2015
19.	*Satureja khuzistanica*	MeJA	Rosmarinic acid	Cell suspension	Khojasteh *et al*., 2016
20.	*Silybum marianum*	MeJA and Cyclodextrin	Silymarin	Cell	Almagro *et al*., 2011
21.	*Stephania venosa*	SA and Chitosan	Dicentrine	Cell suspension	Kitisripanya *et al*., 2013
22.	*Taxus sp.*	MeJA and Cyclodextrins	Taxane	Cell	Sabater-jara *et al*., 2014
23.	*Taxus baccata*	MeJA and Squalestatin	Phenolic content	Cell suspension	Pour *et al*., 2014
24.	*Withania somnifera*	MeJA and SA	Withanolide A, Witholide, Withaferin A	Hairy root	Sevananthum *et al*., 2012

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