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PLANT TISSUE CULTURAL TECHNIQUE TO INCREASE PRODUCTION OF PHYTOCHEMICALS FROM MEDICINAL PLANTS: A REVIEW

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Almost eighty percent of the world inhabitants rely on traditional formulation which obtain by using various medicinal plants to cure and ménage the acute and chronic ailment from the ancient times. Important formulation is made by using the different parts of the plant and the extract of the plant. Number of important phytochemicals present in each plant which we obtained by using several technologies. By using tissue plant culture, we able to obtain desired phytochemicals. These components possess different medicinal activities like antioxidant, anti-inflammatory and many more. Most of the secondary metabolites are obtained from some important herbs. The product which made by using these components are very effective and show fewer side effects. Plant tissue culture is one of the best methods now a days to obtained potential component which usually not derived from the whole plant. *Keywords* : Tissue culture technique, secondary metabolites, medicinal plants, elicitation

Introduction

From the previous decades the history of tissue and plant culture is described in many books, papers and article. Firstly, the tissue culture technique was proposed by Haberlandt Gottlieb in 1902 in which he gave the concept to understand the relation and functionality of cell with different organism. In 1922 first plant is successfully cultured by scientist. For the culture of plant cell, it is important to understand the plant hormone which also known as regulators for the growth of plant. These plant regulators play significance in different manners. 3 indole-butyric acid first growth regulators which discovered in 1926. The period between 1940 to 1960 was a golden period to produce various technique which effectively used for plant tissue culture, these techniques still used for that purpose. At that time various development are done to discover the new and important growth regulator for plant, kinetin was also discovered at that time and it is a good cell division hormone. The scientist of that time Miller and Skoog in 1957 also give concept to understand the control of hormone by adjusting the auxin and cytokines concentration. MS medium also discovered at that time which effectively used for the culture of tobacco cells, this medium consists of C source, low amount of N, macro and micro nutrients, salt concentration high, vitamins obtained from the B complex and growth regulators. From the previous decades to till now researcher do many experiments for the development of important phytochemical and various tissue cultural technique. To get valuable metabolites tissue culture is best for this purpose. By using the tissue culture method for the development of secondary metabolites overcame the development of soil grown plants. The scale up and protocol immobilization allowed the production of secondary metabolites which

effectively used in many applications. Rosmarinus acid and taxol effectively show anti-oxidant and chemotherapeutic characteristics. By using these plant tissue culture number of bioactive components are obtained like phenolic component.

Benefits of using plant tissue culture

Eighty percent of the population depends on natural and plant derivative medicine for their acute or primarily health related issue and it is approved by WHO. It is also proved from the world health organization that almost 2/3 of antiinfectious and anti-carcinogenic medicine which present in market are obtain from plant and their derivatives. Natural plants are very effective for treating number of problems regarding to human health. For the development of important bioactive chemical component tissue culture and plant cell are effective tools in biotechnology and these component used effectively in diversified areas. Tissue culture and plant cells effectively used in the agriculture and food industry to produce component which used in food purpose. These plant derivatives components have potential bioactivity and less toxicity and this one proved from the many researchers. In culturing technique under aseptic tissue situation manipulation of organ cells occurs and the growth of these cells occurs in a culture medium under suitable condition in which controlled light, temperature and humidity present. By using this suitable production system not only increase the extracts standardization and uniformity but also maintain the genetic properties of the colon. In an artificial medium for the maintenance of functions like totipotency and secondary metabolites gene pool is important. The growth rate of plant depends on climate condition, production of secondary metabolites occurs low when environment condition is suitable. production yield improves by using two significant

tools like Biochemistry and biotechnology engineering. Some significant advantages of using tissue culture include controlled and optimized production under suitable condition, final control of product, through genetic engineering selection of best colon, pure compound development, nutritional effect improve, undesired component decrease, pesticides and herbicides production free, chemical synthesis of new component, development not depend on geographic and climate. By using in vitro culture technique plant derivative natural dyes are originated like anthocyanin is an important natural dye. Large scale important bioactive chemical component produced by using meristematic culture (Maria *et al*, 1990). The different types of secondary compounds produced by tissue culture technique and types of traditional medicinal plants are demonstrated in tables -1 and 2.

Table 1 : Secondary metabolites production by plant tissue culture technique

Terpenoids	Alkaloids	Steroids	Quinones	Phenylpropanoids
withanolides	Tropane alkaloids	Lactones steroidal	uglone	tannins
Tri-terpenoid ursane	Tri-gonelline	Glycosides steroidal	thymoquinone	stilbenes
triterpenes	thebaine	scillaridine	shikonin	Pro-anthocyanidins
thapsigargin	piperidine	quabain	rhein	phenalinones
sesterpenes	Iso-quinoline alkaloids	physodine	plumbagin	lignans
sesquiterpenes	Alkaloids indole	helleborin	Phenanthrenequinone	isoflavonoids
paclitaxel	quinolizidine	ecdysteroids	naphthoquinones	Derivative of hydroxycinnamoyl
Mono-terpenes	lobeline	digitoxigenin	Lapachol beta	flavonoids
meroterpenes	Iso-quinolines	digitoxin	emodin	Ferulic acid
ginsenosides	harringtonines	digoxin	chrysophanol	eugenol
di-terpenes	galanthamine	catasterone	benzoquinones	coumarins
cucurbitacins	Furo-quinoline	bufadienolides	anthraquinones	Caffeic acid
artemisinin	betalaines	brassinolide	Aloe emodin	anthocyanins
	acridines			

 Table 2 : Traditional medicinal plants and applications

Medicinal plant	Secondary metabolites	applications
Colocynthis citrullus	Flavonoids, alkaloids, steroids,	It effectively used to cure constipation, edema,
	saponins, curcubitacins	cancer, diabetes, bacterial infection &
		abortifacient.
Bacopa monnieri	Saponins tri-terpenoid	This plant effective in case of epilepsy, memory
		tonic, act as promoter of memory,
		hepatoprotective & anti-oxidant.
Borivilianum chlorophytum	Vitamins, tannins, triterpenoids,	It shows antioxidant & antistress propertiese,
	alkaloids, steroids, sapnins & phenols	show immunomodulatory effect, aphrodisiac
		and as erectile pro agent.
Lobate pueraria	isoflavonoids	It acts as good anti-oxidant, anti-diarrhea, anti-
		pretic, anti-emetic
Wightii commiphora	Mono,di & tri-terpenoids,	It effectively cure the problem related to gout,
	sesquiterpenoids, flavonoids, steroids,	obesity, inflammation, rheumatism and disorder
	lignins and guggultetrols	associated with metabolism of lipid.
Pomifera maclura	Isoflavones prenylated	Shows astringent & fungicodal activities, act as
		natural dye & insect repellant
Perforatum hypericum	Hyperforin and hypericinn	Antiviral, anticancer, anti-depressent, anti-
		inflammatory, neuro-protective, anti-oxidant
		and anti-bacterial
Acurninata camptotheca	10 methoxy & hydroxy camptothecin	Good anti-cancerous agents
Salicifolia heimia	Lythrine, lyfoline, vertine, nesodine,	It shows anti-pyretic, anti-syphilitic, laxative,
	alkaloids, quinolozidine	diuretic and sudorific activities.
Luridus anisodus	Pyridine alkaloids, piperidine and	Effectively shows anti-cholinergic property &
	tropane alkaloids.	act as anaesthatic agent
Belladonna atropa	Tropane alkaloids	It isa good hallucinogenic agent, cure
		parkinsons problem, treat motion sickness &
		ulcer, good anti-inflammatory agent and in case
··· · · ·		of snake bite it is good antidote.
Vulgaris beta	Rhamnoside o2 vitexin, 2-o xyloside	Good natural dye in food industry, anti-
¥ . 1 1.	vitexin, betalains	hypertensive and show hypoglycemic activities.
Lanta digitalis	Ouabain, digoxin, digitoxin, strospeside,	It effectively used to cure congestive heart
	oleandrin, proscillaridin	problem, anti-diabetic, cytotoxic, insecticidal
		and neuro & hepato cardioprotective.

Ginseng panax	ginsenosides	It is act as good tonic for gastro enteric problem	
Dioscorea species	Coumaric acid, phytic acid, allantoin, myricetin, cortisone, discoeine, diosgenin	Anti-tumor, anti-mutagenic, anti-fungal	
Coptis species	Palmatine, berberine, coptisine, jatrorrhizine & epiberberine	Good antidote, neuroprotective, anti- inflammatory and antioxidant	
Catharanthus roseus	Vinblastine, vincristine, serpentine,ajmalicine, vinceine, vinodiline	Effectively treat hodgkins disease, anti- neoplastic, anticancerous & antidiabetic	
Megapotamica baccharis	Baccharine, cinnamic acid, coumarins, flavonoids, diterpenoids, tri-terpenoids oleanane, clerodane	It reduces the phlegm, relieve the cough, anti- viral, anti-neoplastic and induce the diuresis	
Visnaga ammi	Essential oils, pyrones gamma, khellin, visnagin,luteolin, apigeninfurano- chromones	This plant effectively used to cure skin related disorder include psoriasis, vitlligo, effective in case of abdominal cramp & treat renal colic, good vasodilator.	
Rebaudiana stevia	Essential oil, steviol, stevioside and rebaudioside	It effectively used to cure dental caries & IBD, antidiabetic	
Granatum punica	Ellagic acid, flavonoids, phenol, pelletierine	It poasess anti-cancerous activities	
Thymus species	Carvacrol, carotenoids, geraniol, rosmarinic acid, thymol, alpha terpineol	It show activities like Anti-microbial, anti- inflammatory, anti-ulcer, hypoglycemic & gastro-protective	
Filixmas dryopteris	Filixic acid, aspidin, phloroglucinols and deaspidin	Treat the Wound ulcer, anti-inflammatory activities show.	
Citrullus, Cucumis, Cucurbita and Trichosanthes	cucurbitacins	Antiartherosclerotic, antitumor, antidiabetic and anti-inflammatory activities.	
Medusa saussurea	Syringin, gallic acid, tri-terpenoids, phenolic acid, cholenergica cid, rutin,iso-quercitrin, phytosterols and lignins.	Immunosuppressive, hepatoprotective, antiulcer and good antioxidant	
Blumei coleus	Quercetin, eugenol, apigenin, cavacrol, rosmarininc acid	Anti-metastatic, anti-galucomic, cardiotonic, anti-depressent	
Tinctorum rubia	Glycosides, tri-terpenoids, anthraquinones, phytosterols	Good astringent, anti-thrombotic, used for the cure of spleen disorder.	
Parviflora scopolia	Hyoscyamine, scopalamine	Anti-spasmodic & good anti-cholinergic effect	
Taxus species	Taxol, paclitaxel, essential oil,	Anti-microbial, anti-epileptic & aphrodisiac	
Vitis vinifera	Resveratrol, querecetin, stilbene, kaempferol, flavonol, iso-rhamnetin & epicatechin	Diuretic, purgative, anti-anxietic and anti- thromotic activities.	
Rauwolfia species	Reserpilline, alstonine, carboline beta, serpentine, solanine alpha, ajmaline	Effectively used to menage schizophrenia, epilepsy, insomnia and hypertenstion	
Ephedra	Pro-anthocyanidines, leuco- anthocyanidine, leuco-pelargonine, alkaloids ephedrine	It is a good appetite suppression	
Datura stramonium	Tropane alkaloids	Relieve the pain of gout and rheumatism.	
Tinctorius carthamus	Alkaloids, lignans, phenolics, carboxylic acid, glycosides C, steroids	Anti-coagulant, effective in case of cerebrovascular disease	
Ginkgo biloba	Kaempferol, quercetin, ginkgolide A, ginsenoside	Anti-diabetic and anti-inflammatory activities	
Ruta species	Acridone, flavonoids, quinolone alkaloids	Natural pesticides & fungicidal	
Doryphore dioscorea	diosgenin	Hypercholesterolemia, effective for cancer therapy.	

Tissue culturing and plant cell for medicinal plants

Tissue culture and plant cell used as alternative medium for the faster propagation of plant and also produced those phytochemicals which are disease preventive obtained from the medicinal plants. Many species of plant produced by using various in vitro approaches like these species produced from a tissue, organ or single cell which is known as explant. Under sterile situation these technologies are developed from any vegetative part and plant organs include stems, root, leaves, axillary, nodes, meristem, embryo, endosperm etc. clonal and micro propagation of plant is also vegetative propagation in which cultivars multiplication occurs of those whose genetically copies are identical. By using these propagations every year not only thousand but also millions of copies are produced. With the passage of time this technique used for the selection of colon and produce those material which are disease free. This micro-propagation technique used for various plants like Camellia sinensis, Chinens allium, Cardamomum elettaria, Aremisia annua, Rebaudiana stevia, Panax, Cathranthus roseus, and Chiravita swertia. Some other important herb also propagated by using these techniques (Erdei et al., 1981; Hiraoka et al., 1986; Sagare et al., 2000; Pradhan et al., 2013). This technique used to develop various important phytochemical (Yamada et al., 1991). Plant tissue culture have potential to produce bioactive chemical metabolites from the traditional plants (Ramachandra and Ravishankar, 2002; Dornenburg, 2010; Salim et al., 2019a). Totipotent are plant cell in culture which produce same chemical metabolites as produced from the whole plant. For the development of metabolites from the plant culture many advancements are done in this field. This way is convenient more than any other because in this we develop beneficial component under suitable condition. secondary metabolites production by using conventional biotechnology method include regulator growth composition, condition of environment and changing composition of nutrient. Number of techniques used for the development of maximum secondary metabolites and these techniques are elicitation, immobilization of cell and metabolic engineering. Different phytochemicals and ingredients of food like sweeteners, essential oils, colorants, nutraceuticals, flavors and antioxidant produced using cell culture (Dornenburg, 1996; Ushiyama, 1996; Abdin and Kamaluddin, 2006).

Types of culture

By using different method in culture system for the development of important chemical metabolites, with the passage of time these strategies gain more important (Dornenburg and Knorr, 1997). Various culture used to gain useful metabolites and these include transform of organ and cell, immobilized cell, cell suspension, callus and organized tissues (Salim *et al.*, 2019b).

Tissue organized cultures

Different parts of plant used in organ culture technique like root, shoot and many more for the development of desired component that required in the differentiation of cells. Development of secondary metabolites from the tissue organized culture is vary from the other intact plant, development of chemical metabolites and stable growth concentration sometimes equal or higher observed in the root and shoot culture of various species (Endo and Yamada, 1985; Li et al., 2009; Salim et al., 2020). Most of time those components which are not found in whole plant, detected in cultured tissues. The cultured roots of Cepharantha stephania possess high level of alkaloids than the other plant parts and aromoline which originally not present but detected in cultured plant (Sugimoto et al., 1988). Tanshinones alkaloids which obtain from the Salvia miltiorrhiza root culture important Chinese traditional medicine under appropriate situation (Shimomura et al., 1991). Number of important phytochemicals are obtained from the Corydalis yanhusuo (Lee et al., 2001). Tubers of plant derivative somatic embryo possess significant bioactive component kike corydaline D and tetra-hydropalmatine L, D. large number of alkaloids are obtained from the cutting of small bulbs of Fritillaria unibracteata which propagated rapidly and

possess useful microelements (Chueh et al., 2000; Gao et al., 2004).

Cell suspension and callus culture

From any type of explants un-differentiated mass developed in culture is known as callus. In suspension culture of cell homogenous suspension divide rapidly in nutrient liquid media. In liquid media callus is suspended, in cell suspension culture. After that, suspension of cell placed in a shaker which allow the aggregated of cell vanish and form smaller clumps and single cell which evenly divide and grow continuously in liquid media (George et al., 2008). Plant suspension culture give an important platform for the development of important chemical metabolites (Wickremesinhe and Arteca, 1993; Paudel et al., 2013). By using these cultures important component like codeine and morphine are derived from the Papaver somniferum (Furuya et al., 1972; Yoshikawa and Furuya, 1985). An important anti-cancerous drug is taxol which approved from the drug and food administration that effectively used to cure the breast and ovarian cancer (Wickremesinhe and Arteca, 1994). The development of taxol occurs via species of Taxus which commercially very important (Cragg et al., 1993; Srinivasan et al., 1995). In suspension culture paclitaxel yield at high level from T. brevifolia cell (Kim et al., 1995; Lee et al., 1995). From the callus culture of Camptotheca acuminata an important metabolite like camptothecin was obtained (Van Hengal et al., 1992).

Development of secondary metabolites from different systems

With the passage of time many advancements are done in tissue culture techniques when combined with genetic engineering then it gives high potential nutraceutical and pharmaceutical which are important useful component (Furuya et al., 1984). Further important chemical metabolites are produced by using various bio-reactors, also these bioreactors used for the commercial development of secondary metabolites (Hansen and Wright, 1999). To scale up the chemical metabolites different culture systems are present like immobilization of cell an important technique which fix the cells of plant in a suitable matrix. This technique act as a protector for plant cell against mechanical stress. Immobilization technique is significantly used to produce extracellular metabolites, also important ingredient of food synthesized by using this technique. Various important medicinal plants which developed through culture system not only un-differentiate the culture of cells but also induce organized specific culture (Cheetham, 1995; Valluri, 2009).

Elicitation

In plants the synthesis of chemical metabolites and phytoalexins stimulate by using elicitors component. Cultures of cells are of two types like abiotic and biotic, in biotic culture present *Aspergillus niger* and chitin crude, but in abiotic culture include jasmonate methyl, mannitol. Elicitors are microbial and plant polysaccharides, material of fungal wall and chemical which enhance the synthesis of secondary metabolites from different cells of the plant and tissue culture. The most commonly used elicitors include extract of yeast, chitosan, fungal carbohydrates, these are effective elicitors to produce phytochemicals by using plant species (Verma *et al.*, 2012). The synthesis of anthraquinone increases by using abiotic elicitor which is chitosan (Jin *et al.*, 1999; Wink *et al.*, 2008). By using these elicitors not only yield of secondary metabolites increase but also food ingredient enhances (Zhao *et al.*, 2001; Salim *et al.*, 2019a).

Transformed tissue culture

With the passage of time technology contribute a lot in the development of phytochemicals, because these phytochemical shows beneficial effects on human health. For the good production of chemical metabolites root hairy transgenic culture used which is mediated and transformed by *Agrobacterium rhizogenes* (Karuppusamy, 2009; Li *et al.*, 2011). This culture unique in stability point of view, rapidly growth occur and maintained of this technique is easy (Shanks and Morgan, 1999; Asano *et al.*, 2013). The growth rate of hairy root culture is more than un-transformed shoots and roots (Flores *et al.*, 1987). So, transformed roots have ability to produce more secondary metabolites than their parent plants (Spencer *et al.*, 1990; Giri and Narasu, 2000).

Metabolic engineering

This technique is mostly applied to improve the synthesis of various chemical metabolites in several cultures (Van-Pee, 2001). In an organism metabolic alteration occur by using metabolic engineering to attain good cellular pathway for the transformation of chemical and regulate the cell function by using deoxyribonucleic acid technology (Kinney, 1998). By using these techniques, we attain desired metabolites via direct cellular metabolism (Sato *et al.*, 2001).

Conclusion

From the ancient times medicinal plant effectively used in traditional medicine. The production of phytochemicals and secondary metabolites from plant tissue cultures are very beneficial for various diseases include acute and chronic. Plants are rich sources of chemical component, these bioactive components include number of nutraceutical and pharmaceutical component which have potential to protect human related problem. For the improvement and development of metabolites obtain by using various strategies.

References

- Abdin, M.Z. and Kamaluddin, A. (2006). Traditional systems of medicine: improving quality of medicinal herbs through physico-chemical and molecular approaches. India Publishing House Pvt. Ltd, New Delhi.
- Asano, T.; Kobayashi, K.; Kashihara, E.; Sudo, H.; Sasaki, R.; Iijima, Y.; Aoki, K.; Shibata, D.; Saito, K. and Yamazaki, M. (2013). Suppression of camptothecin biosynthetic genes results in metabolic modification of secondary products in hairy roots of Ophiorrhiza pumila. Phytochemistry, 91:128–139.
- Cheetham, P.S.J. (1995). Biotransformations: new routes to food ingredients. Chem. Ind., 7:265–268.
- Chueh, F.S.; Chen, C.C.; Sagare, A.P. and Tsay, H.S. (2000). Quantitative determination of secoiridoid glucoside in in vitro propagated plants of Gentiana davidii var. formosana by high performance liquid chromatography. Planta Med., 67:70–73.
- Cragg, G.M.; Schepartz, S.A.; Suffuess, M. and Grever, M.R. (1993). The taxol supply crisis: new NCI policies for handling the large-scale production of novel natural

product anticancer and antiHIV agents. J. Nat. Prod., 56:1657–1668.

- Dörnenburg, H. (2010). Cyclotide synthesis and supply: From plant to bioprocess. Biopolymers Pept. Sci., 94(5):602–610.
- Dörnenburg, H. and Knorr, D. (1996). Generation of colors and flavors in plant cell and tissue cultures. Crit. Rev. Plant. Sci., 15:141–168.
- Dörnenburg, H. and Knorr, D. (1997). Challenges and opportunities for metabolite production from plant cell and tissue cultures. Food Technol., 51:47–54.
- Endo, T. and Yamada, Y. (1985). Alkaloid production in cultured roots of three species of Duboisia. Phytochemistry, 24:1233–1236.
- Erdei, I.; Kiss, Z. and Maliga, P. (1981). Rapid clonal multiplication of Digitalis lanata in tissue culture. Plant Cell Rep., 1:34–35.
- Flores, H.E.; Hoy, M.W. and Pickard, J.J. (1987). Secondary metabolites from root culture. Trends Biotech., 5:64–69.
- Furuya, T.; Ikuta, A. and Syono, K. (1972). Alkaloids from callus cultures of *Papaver somniferum*. Phytochemistry, 11:3041–3044.
- Furuya, T.; Yoshikawa, T.; Orihara, Y. and Oda, H. (1984). Studies of the culture conditions for Panax ginseng cells in jar fermenters. J. Nat .Prod., 47:70–75.
- Gao, S.L.; Zhu, D.N.; Cai, Z.H.; Jiang, Y. and Xu, D.R. (2004). Organ culture of a precious Chinese medicinal plant—*Fritillaria unibracteata*. Plant Cell Tiss. Org. Cult., 59:197–201.
- George, E.F.; Hall, M.A. and DeKlerk, G.J.(2008). Plant Production by Tissue Culture. Volume 1. The Background, 3rd Edition, Published by Springer, Dordrecht, The Netherland.
- Giri, A. and Narasu, M.L. (2000). Transgenic hairy roots: recent trends and applications. Biotech. Adv., 18:1–22.
- Hansen, G. and Wright, M.S. (1999). Recent advances in the transformation of plants. Trends Plant Sci., 4:226–231.
- Hiraoka, N.; Kodama, T.; Oyanagi, M.; Nakano, S.; Tomita, Y.; Yamada, N.; Iida, O. and Satake, M. (1986). Characteristics of Bupleurum falcatum plants propagated through somatic embryogenesis of callus cultures. Plant Cell Rep., 5:319–321.
- Jin, J.H.; Shin, J.H.; Kim, J.H.; Chung, I.S. and Lee, H.J. (1999). Effect of chitosan elicitation and media components on the production of anthraquinone colorants in madder (*Rubia akane* Nakai) cell culture. Biotech. Bioprocess Eng., 4:300–304.
- Karuppusamy, S. (2009). A review on trends in production of secondary metabolites from higher plants by in vitro tissue, organ and cell cultures. J. Med. Plants Res., 3:1222–1239.
- Kim, J.H.; Yun, J.H.; Hwang, Y.S.; Byun, S.Y. and Kim, D.I. (1995). Production of taxol and related taxanes in *Taxus brevifolia* cell cultures. Biotech. Lett., 17(1):101–106.
- King, P.J .(1984). Induction and maintenance of cell suspension cultures. In: Vasil IK (ed) Cell Culture and Somatic Cell Genetics of Plants. Academic Press, New York.
- Kinney, A.J. (1998). Manipulating flux through plant metabolic pathways. Curr. Opin. Plant Biol., 1:173– 178.

- Lee, C.Y.; Lin, F.L.; Yang, C.T.; Wang, L.H.; Wei, H.L. and Tsay, H.S. (1995). Taxol production by cell cultures of *Taxus mairei*. In: Proceedings of symposium on development and utilization of resources of medicinal plants in Taiwan.
- Lee, Y.L.; Sagare, A.P.; Lee, C.Y.; Feng, H.T.; Ko, Y.C.; Shaw, J.F. and Tsay, H.S. (2001). Formation of protoberberine-type alkaloids by the tubers of somatic embryo-derived plants of *Corydalis yanhusuo*. Planta Med., 67:839–842.
- Li, M.; Peebles, C.A.; Shanks, J.V. and San, K.Y. (2011). Effect of sodium nitroprusside on growth and terpenoid indole alkaloid production in *Catharanthus roseus* hairy root cultures. Biotech. Prog., 27(3):625–630.
- Li, W.; Li, M.; Yang, D.L.; Xu, R. and Zhang, Y. (2009). Production of podophyllotaxin by root culture of *Podophyllum hexandrum* Royle. Electron J. Biol., 5:34– 39.
- Maria, I.D.B.; Maria, J.S.; Rita, C. A. and Isabel, C.F.R. F. (1990). Exploring plant tissue culture to improve the production of phenolic compounds: A review. In: Mountain Research Centre (CIMO), ESA, Polytechnic Institute of Bragança, Campus de Santa Apolónia, 1172, 5301-855 Bragança, Portugal. bREQUIMTE/LAQV, Departamento de Ciências Químicas, Faculdade de Farmácia da Universidade do Porto, Rua Jorge Viterbo Ferreira, 228, 4050-313 Porto, Portugal.
- Paudel, S.; Adhikari, S.R. and Pant, B. (2013). Effect of colchicine on production of secondary metabolites from callus of *Withania somnifera* (L.) Dunal. J. Nepal Biotech. Assoc., 3(1):15–18.
- Pradhan, S.; Paudel, Y.P. and Pant, B. (2013). Efficient regeneration of plants from shoot tip explants of *Dendrobium densiflorum* Lindl., a medicinal orchid. Afr. J. Biotech., 12(12):1378–1383.
- Ramachandra, R.S.and Ravishankar, G.A. (2002). Plant cell cultures: chemical factories of secondary metabolites. Biotech. Adv., 20:101–153.
- Sagare, A.P.; Lee, Y.L.; Lin, T.C.; Chen, C.C. and Tsay, H.S. (2000). Cytokinin-induced somatic embryogenesis and plant regeneration in *Corydalis yanhusuo* (Fumariaceae) a medicinal plant. Plant Sci., 160:139– 147.
- Salim, S. A.; Hamza, S.Y. and Habeeb, M.S. (2019a). Enhancement of *Gardenia jasminoides* Ellis friable callus growth and its constituents of some bioactive compounds. Plant Arch., 19 Supplement 2:398-402.
- Salim, S.A.; Abood, K.H. and Razzooqee, M.A. (2019b). Determination of secondary metabolites in callus and different tissues of *Physalis angulate* L. Res. Crops, 20(3):642-647.
- Sato, F.; Hashimoto, T.; Hachiya, A.; Tamura, K.; Choi, K.B. and Morishige, T. (2001). Metabolic engineering of plant alkaloid biosynthesis. Proc. Nat. Acad. Sci., 2:367–372.
- Shanks, J.V. and Morgan, J. (1999). Plant hairy root culture. Curr. Opin. Biotech., 10:151–155.
- Shimomura, K.; Kitazawa, T.; Okamura, N. and Yagi, A. (1991). Tanshinone production in adventitious roots and regenerates of *Salvia miltiorrhiza*. J. Nat. Prod., 54:1583–1586.

- Spencer, A.; Hamill, J.D. and Rhodes, M.J.C. (1990). Production of terpenes by differentiated shoot of *Mentha* citrate transformed with *Agrobacterium tummifacience* T-37. Plant Cell Rep., 8:601–604.
- Srinivasan, V.; Pestchanker, L.; Moser, S.; Hirasuma, T.; Taticek, R.A. and Shuler, M.L. (1995). Taxol production in bioreactors; kinetics of biomass accumulation, nutrient uptake, and taxol production by cell suspensions of *Taxus baccata*. Biotech. Bioeng., 47: 666–676.
- Sugimoto, Y.; Sugimura, Y. and Yamada, Y. (1988). Effects of culture conditions on roots of *Stephania cepharantha*. Agric. Biol. Chem., 52:1495–1498.
- Ushiyama, K. (1996). Commercial production of ginseng from plant cell cultures. Institute of Food Technologists Annual Meeting, New Orleans.
- Valluri, J.V. (2009). Bioreactor production of secondary metabolites from cell cultures of periwinkle and sandalwood. Methods Mol. Biol., 547:325–335.
- Van Hengal, A.J.; Harkes, M.P.; Witchers, H.J.; Hesselinic, P.G.M. and Buitglaar, R.M. (1992). Characterization of callus formation and camptothecin production by cell lines of *Camptotheca acuminata*. Plant Cell Tiss. Org. Cult., 28:11–18.
- Van Pee, K.H. (2011). Transformation with tryptophan halogenase genes leads to the production of new chlorinated alkaloid metabolites by a medicinal plant. Chem. Biochem., 12(5):681–683.
- Verma, P.; Mathur, A.K.; Srivastava, A. and Mathur, A. (2012). Emerging trends in research on spatial and temporal organization of terpenoid indole alkaloid pathway in *Catharanthus roseus*: literature update. Protoplasma, 249(2):255–268.
- Wickremesinhe, E.R.M. and Arteca, R.N. (1993). *Taxus* callus cultures: initiation, growth optimization, characterization and taxol production. Plant Cell Tiss. Org. Cult., 35:181–191.
- Wickremesinhe, E.R.M. and Arteca, R.N. (1994). *Taxus* cell suspension cultures: optimizing growth and production of taxol. J. Plant Physiol., 144:183–188.
- Wink, M.; Alfermann, A.W.; Franke, R.; Wetterauer, B.; Distl, M. and Windhovel, J. (2008). Sustainable bioproduction of phytochemicals by plant in vitro cultures: anticancer agents. Plant Genetic Resou., 12:113–123.
- Yamada, Y.; Shoyama, Y.; Nishioka, I.; Kohda, H.; Namera, A. and Okamoto, T. (1991). Clonal micropropagation of *Gentiana scabra* Bunge var. buergeri Maxim and examination of the homogeneity concerning the gentiopicroside content. Chem. Pharm. Bull., 39:204– 220.
- Yoshikawa, T. and Furuya, T. (1985). Morphinan alkaloid production by tissues differentiated from cultured cells of *Papaver somniferum*. Planta Med., 2:110–113.
- Zhao, J.; Hu, Q.; Guo, Q. and Zhu, W.H. (2001). Effects of stress factors, bioregulators, and synthetic precursor on indole alkaloid production in compact callus clusters cultures of *Catharanthus roseus*. Appl. Microbial Biotech., 55:693–698.