Plant Archives Vol. 20, Supplement 2, 2020 pp. 3385-3391 **e-ISSN:2581-6063 (online), ISSN:0972-5210**

BIOTIC ELICITATION: A TOOL FOR PRODUCING BIOACTIVE COMPOUNDS

Nisha Kumari, Biji A. Varghese, Minhaj Ahmed Khan, Surender Jangra*, Arvind Kumar*
School of Bioengineering and Biosciences, Lovely Professional University, Punjab, India
Corresponding author (arvind_ldl@rediffmail.com; surender.21627@lpu.co.in)

Abstract

Primary metabolite has a vital function in growth of the plant. They play an effective role in all essential processes of plants such as respiration, photosynthesis. Secondary metabolites are organic molecules. They play no role in the growth and development of plant bodies. In the absence of secondary metabolites, plant starts to die. Generally, secondary metabolites play a vital role in defense of the plant. Compound which stimulates all type of physiological abnormality of plants are called Elicitors. Elicitors can be released either from plant or pathogen. Plant based elicitors are called as endogenous elicitors and pathogen based elicitors are called exogenous elicitors. Elicitor can also be classified as abiotic and biotic elicitors. The elicitors that have biological origin are called biotic. They are derived from plant itself or from pathogen. Biotech approach for example plant tissue culture is playing an important function in research for substitutes to the production of desirable medicinal compound from the plant. In this review we will discuss the importance of secondary metabolites and elicitors in the metabolism of plant and their production using plant tissue culture.

Keywords: Elicitors, Secondary Metabolites, Metabolism, Plant Tissue Culture

Introduction

Plants are made from plants constituents and they are the individual chemicals from which they made. They are organic in nature (Singh *et al.,* 2019). By the activity of individual cells, they synthesized in plants. Plant constituent are complex organic chemical constituents by utilizing enzymes and simple substances formed by the process called biosynthesis (Harborne, 1988). The chemistry of secondary metabolites is made up from organic compounds. For the normal metabolism of the organisms, they are not directly responsible. That's why, these organic compounds are known as secondary-metabolite. The secondary metabolite is complex organic molecule. The secondary metabolites are biosynthesized through the primary plant metabolites in the plant cells. They usually possess the many activities, which are neither required to sustain plants nor to provide energy. But it is probably synthesized to defensive goals (Hadacek, 2002).

Researchers are intensively studying the constituents of plants and their various nutritional importance from decades. Metabolism is the process by which plants produce various products and intermediates known as the 'metabolites' of plants. Primary metabolites such as carbohydrates, lipids and amino acids are produced. In addition to this, higher plants also synthesize various low molecular weight compounds called secondary metabolites that establish the defense mechanism in them (Wang and Wu, 2013; Chauhan *et al.,* 2018).

Secondary metabolite is organic molecule. It has no role in the normal growth (Gupta *et al.,* 2014). Also no role in the development of organisms. But primary metabolite has a vital function in growth of the species. They play an effective role in respiration and also in photosynthesis in the plants. When secondary metabolite is absent, then the plant is not turn to actual death. However, the result is long period destruction of survivability of the organisms, generally they are playing vital role in defense of the plant. These compound is an acutely distinct class of natural products which is synthesize by plants, animals, algae, fungi, and bacteria. The secondary metabolites like alkaloids, phenolic compound and terpenes are divided on the bases on origin of their biosynthesis. Distinct divisions of the compounds are mostly combined with narrow set of species within a phylogenetic group and constitute the photochemical in the various colorant, spice plants, aromatic and functional foods (Roze *et al.,* 2011; Sirohi *et al.,* 2014).

Whereas plant secondary metabolite is primarily combined with plant defense feedback across/against herbivore and pathogen and these different compound can be involving in a large cluster of the ecological function (Bertin *et al.,* 2003). Secondary compound is released by plants into their environment that change chemistry of soil (Gupta *et al.,* 2014). So they increase uptake of nutrients and defending against the metal toxicity (Dakora and Phillips, 2002). Chemical signal is necessary for resolving interaction among non-pathogenic bacteria of soil and roots of plant, along with di nitrogen (N_2), S fixing bacterial symbionts (Dakora and Phillips, 2002; Marx, 2004).

Diversity of mechanisms are used by the plants to discharge secondary compound as volatile, such as compounds which generate scent correlated with a pungent leaves and flowers, whereas roots also can actively release volatile (Steegh *et al.,* 2004). Thirty percent of the plant photosynthetic activity is used for the synthesis of root exudates. And it affects the local soil environment which is term as rhizosphere. All of the processes may be discharge chemical that are mediating allelopathic interaction among the plants (Bertin *et al.,* 2003). Some constituents of the plants are considered as inactive constituent as they don't provide therapeutic importance. Some constituents are involved in development, reproduction and growth of plants and they are considered as active constituent (Amit *et al*., 2014). The formation of inactive and the active constituents of plant involve distinct metabolic pathways. Active constituents are considered as primary plant metabolites inactive are considered as plant secondary metabolite (Stamp and Nancy, 2003). Unlike primary metabolite of the plant, existence of secondary metabolite is generally playing a vital role in plant defense system (Osbourn *et al.,* 2003).

Compound which stimulates all type of physiological abnormality of plants is called Elicitors (Radman *et al.,* 2003). Elicitors can be released either from plant or

pathogen. Plant based elicitors are called as endogenous elicitors and pathogen based elicitors are called exogenous elicitors. Endogenous elicitors are released from the plant when attacked by pathogens. Secondary metabolite can be raised from these elicitors. They can act vital role in production of commercially necessary compound (Handa *et al.,* 2019). The secondary metabolite is discharged because of the defense responses that activated and caused through elicitor, signal compounds of plant defense response (Radman *et al.,* 2003).

As per Radman *et al.,* 2003 elicitors are divided into two classes that is physical and chemical. Elicitor can also be classified as abiotic and biotic elicitors. The elicitors that have biological origin are called biotic. They are derived from plant itself or from pathogen. And abiotic elicitor has not a biological origin. They are classified into chemical compounds and physical factor. The very first biotic elicitor invented in 1968. It may be divided into general elicitors and race specific on the basis of plant elicitor interaction (Staskawicz *et al.,* 1991). There are distinct plant hormones that are acting as Elicitor. Most common plant hormone such as JA and Salicyclic acid (SA). Both are crucial signal for defense gene expression. SA is regulating resistance to pathogen such as fungal, viral or bacterial. JA controls the protein production through the octadecanoid pathway. JA and SA both are synthetic mimic. They could be applied externally to activate metabolic pathway that provides protection against pathogens. The biochemical pathway of JA and SA both helpful in plant elicitation process of the plant (Angelova *et al.,* 2006).

Polysaccharide chitosan is an example of biotic elicitor which is used in this research. Basically, chitosan is an important derivative of chitin. Chitosan is a polymer of β-1,4-D-glucosamine which is derived from crab-shell chitin. The chitosan use is limited due to its high viscosity, insolubility in water and at high pH it has tendency to coagulate with proteins. It is nontoxic, inexpensive and possesses reactive amino groups. Chitosan is proved to be beneficial in many various, helpful in plant defensive responses, antimicrobial compound in agriculture, as a flocculating agent in WTP, as a hydrating agent in cosmetics, as as food additive and more recently it is used as pharmaceutical agent in biomedicine (Rabea *et al.,* 2003).

Classification of secondary metabolites

Secondary metabolite from the plant could be classified into 3 chemically various group that is Phenolic, Terpenes and N and S containing compound.

Terpene

Terpene are biggest class of the secondary metabolite. They are concerted through their simple biosynthetic origin from glycolytic intermediates or acetyl coenzyme A (Gershenzon *et al.,* 1991; Fraga, 1988; Gupta *et al.,* 2013). A big majority of various terpene structure produced through the plant as secondary metabolite that acts as toxins or feeding deterrent to a huge number of plant feeding mammals and insects (Gershenzon *et al.,* 1991).

Monoterpene (C10)

Number of derivative are vital agent of the insect toxicity. Pyrethroid (monoterpene ester) present in the flower and leaves of the Chrysanthemum species, and shows the insecticidal activities against insects like moths, bees, wasps etc (Gupta *et al.,* 2013). It is very famous additive in commercial insecticide due to low mammalian toxicity and low persistence in the environment (Turlings *et al.,* 1995). In Gymnosperm like Pine monoterpene assemble in resin duct found in twings, needle and trunk specially as β-pinene, α-pinene, myrecene and limonene. All are toxic to diverse insect including bark beetles (Turlings *et al.,* 1995).

Sesquiterpene (C15)

Till now, many sesquiterpene has described for their important role in plant defense like costunolide is anti herbivore agent of family complex characterizes by five membered lactone ring and big repel most mammals and insects from eating (Picman, 1986). ABA, a sesquiterpene, plays important role in maintenance and initiation of seed and bud dormancy, and acting as a transcriptional activator (Mccarty *et al.,* 1991). Also, it enhances the concentration of calcium in the cytoplasm and causes the alkalinisation (Irving *et al.,* 1992). In response to ABA, levels of quercetin, kaempferol and flavonols enhanced significantly. Levels of cinnamic acid, ferulic acid and caeffic acid also increases in response to ABA. All of the change, in protective compound, anti-oxidant enzymatic activities and sterol corresponded with decrease membrane damage through UltraViolet-B. Hence, defense system of plants against UltraViolet-B is stimulated in which ABA acting as downstream in signaling pathways (Berli *et al.,* 2010).

Diterpene (C20)

Abietic acid, example of diterpene. It is found leguminous and pine trees (Sharma & Parihar, 2014). They are found in resin in resin canals of the tree trunk. When, canal is broken through feeding insect, the discharge be of resin may be substantially block the feeding and deliver as a chemical deterrent to continued predation. Another example is phorbol is found in plants of Euphorbiaceae (Dipika *et al.,* 2018). It works as internal toxins to mammals and skin irritants. Furthermore, phytol is a more hydrophobic 20-Carbon alcohol found in the chlorophyll as a side chain helping to anchor certain molecule in membrane. That's why, enhances efficiency of the chlorophyll at time of the photosynthesis (Knoff, 1991), biomass production and the strategy for the highest carbon dioxide fixation (Jagendorf, 1967).

Triterpene (C30)

Steroid alcohols or sterols are vital components of cell membrane in plants, specially in the plasma membrane they act as a regulatory channel. By reducing the motion of the fatty acid chain, they control the permeability to smallers molecules. The milk weeds produce distict good tasting glucosides or sterols that protects them against herb ivory (Lewis *et al.,* 1977)

Polyterpene (C5)

Certain higher molecular weight polyterpene appear in the plant. Largest terpene includes polyterpene and tetraterpene. The main tetra terpenes belong to carotenoid family of pigment. Example of polyterpene is rubber. Rubber is a polymer. It contains 1500-15000 isopentenyl unit (Eisner and Meinwald, 1995).

Phenolic compound

Plant produces huge diversity of the secondary product or metabolite, accommodate phenol group. Phenol group is

chemical heterogeneous group (Prasad *et al.,* 2010). They can be vital component of plant defense against disorder like root parasitic nematodes and pest (Savirnata *et al.,* 2010).

Coumarin

Coumarin is simple phenolic compound. Their function is to act in different plant defense mechanism against fungi, insects and herbivores. Coumarin is derived from the shikimic acid pathway. Common in fungi, plants and bacteria, but not present in the animal. Coumarin is higher active class of molecule with the broad range of antimicrobial activity against bacteria and fungi (Brooker *et al.,* 2008).

Furano-coumarin

It is a category of coumarin with appropriate interest of phytostoxicity. They are not toxic. Untill, they stimulated through UltraViolet-A light. They cause few furano-coumarin to become stimulated to highly energy electronic state. They can be insert into the double helix of Deoxyribonucleic acid. And binds to the pyramidine base (Kesarwani *et al.,* 2013). Thus blocks transcription and finally leading to cell death (Rice and Elroyleon, 1984; Singh *et al.,* 2016).

Lignin

Lignin is highly branched polymer of phenyl propanoid group. It is formed by 3 distinct alcohols that is coumaryl, sinapyl and coniferyl (Bhatt, 2012). That are oxidized to free radical through a ubiquitous plant enzyme for example peroxidise enzyme. This enzyme acts together and random to form lignin (Lewis and Yamamoto, 1990). Lignification blocks growth of the pathogen. They gave frequent response to wounding or infection (Gould, 1983).

Flavonoid

Flavonoid is one of the biggest class of plant phenolic compound. They perform very distinct function in the plant system includes defense and pigmentation (Kondo *et al.,* 1992; Tanwar & Modgil, 2012). 2 another big group of flavonoid occur in flower. These group are flavonols and flavones. Their action is to save cell from the UltraViolet-B radiations (Lake *et al.,* 2009). Exposure of plant to enhanced UltaViolet-B light is determined to enhance the synthesis of the flavonols and flavones suggesting that flavonoid may be attempt measure of the protection through screening out dangerous UltaViolet-B radiations (Savirnata *et al.,* 2010; Caldwell *et al.,* 1983; Batra *et al*., 2013)

Sulphur containing secondary metabolite

Sulphur containing secondary metabolite includes GSL, phytoalexins, GSH, allinin and thionin that is combined indirectly or direct with defense of the plants against microbial pathogen (Crawford *et al.,* 2000; Hell, 1997).

Glutathione (GSH)

In the soluble fraction of the plant, GSH is one of the biggest class of the organic sulphur. In the regulation of plant growth and development, it is playing vital role as mobile pool of shortened sulphur (Kang and Kim, 2007).

Glucosinolates (GSL)

GSL is a class of light molecular mass nitrogen and sulphur contains plant glucoside which is formed through higher plants to enhance their resistance against unfavourable effects of competitor, parasite and predators due to their break down product is discharge as volatile defensive substance exhibiting toxic or repellent effects for example, mustard oil allyl cys sulfoxides in allium and glucosides in cruciferae (Leustek, 2002).

Nitrogen containing secondary metabolite

Nitrogen containing secondary metabolite are cyanogenic glucoside, alkaloids and non protein amino acid. Mostly, they are biosynthesizing by common amino acid. All are important due to their act in anti herbivore defense and toxicity to human.

Alkaloid

Alkaloid includes secondary metabolite containing nitrogen. 20 percent of the vascular plants are having these kind of secondary metabolites (Hegnauer, 1988). Broadly, they include the pyrrolizidine alkaloids. They are toxic. They provide protection against microorganisms and herbivorous attacks. The source of these kinds of metabolites are few common amino acids such as tryptophan, tyrosine, aspartic acid and lysine (Pearce *et al.,* 1991).

Cyanogenic glucoside

They made group of nitrogen containing defensive compound other than alkaloid, releases poison HCN. Mostly occurs in member of family like Graminae and Rosaceae (Seigler, 1981). In native form they are non-poisonous but when they are broken down, they produce the volatile poisonous substance like H2S and HCN. Presence of these blocks feeding by insect and other herbivore like slug and snails (Taiz and Zeiger, 1995).

Plant Tissue Culture as a source for the Secondary Metabolite production

Tissue culture and plant cell can establish generally under the sterile circumstances from the explant like stem, plant leaf, roots etc. for both approaches for the extraction and multiplication of secondary metabolite. Earlier, to treat health disorders in human and infection and illness plant with secondary metabolite is used (Prabhakar *et al.,* 2013). In the previous 100 years, natural products are replaced by synthetic drug. Mostly, higher plant is main source of useful secondary metabolite, used in medicine industry, aroma and flavour industries (Phillipson, 1990). Biotech approach for example plant tissue culture is playing an important function in research for substitutes to the production of desirable medicinal compound from the plant (Ravishankar *et al.,* 1988). Medicinal plant is mainly used as crude drug and extract on a global scale. Various compounds including many alkaloids like codeine (antitussive), morphine (act as pain killer), ephedrine (stimulant), papaverine (phosphor-diesterase inhibitor), ajmaline (antirrhythmic), reserpine (antihy-pertensive), quinine (antimalarial), scopolamine (travel sickness), galanthamine (acetylecholine esterase inhi-bitor), caffeine (stimulant), berberine (psoria-sis).

Production of secondary metabolite from medicinal plant through plant tissue culture

Taxol

Plaxitaxol or Taxol is complex di-terpene alkaloid. Taxol occurs in bark of the Taxus tree. Taxol, most s important anti-cancer agent. It is known for its various way of action at micro tubular cell system (Jordon and Wilson,

1995). Production of taxol through by plant cell culture technique is one of the most broadly research sectors because of the excessive industrial value of taxol, lack of the Taxus tree, and expensive synthetic process (Suffness, 1995). In 1989, first time the production of placlitaxel (taxol) through Taxus cell cultures reported.

Morphine and Codeine

Morphine and codeine are produced from the latex of *Papaver somniferum* and using plant tissue culture techniques their production has also been reported (Yoshikawa and Furuya, 1985; Tam *et al.,* 1980).

Ginsenoside

The root of Panax ginseng is called ginseng. It has been generally using as high prized medicine (Tang and Eisenbrand, 1992). Ginseng is re-cognized as factor for longevity and health. The essential bioactive component of ginseng was identified as ginsenoside that is class of triterpenoid saponins.

L-3,4-dihydroxyphenylalanine

In higher plants, it is the vital medium of secondary metabolite metabolism. It is the source of betalain, melanine and alkaloid isolated from the Vinca faba, Baptisia, Mucuna and Lupinus. Also, it is a messenger of catecholamine in animal. For Parkinson's disease this is used as potent drug (Guggenheim, 1913).

Berberine

It is an isoquinoline alkaloid. It is occurring in cortex of *Phellondendron amurense* and roots of *Coptis japonica*. These are antibacterial alkaloid (Prabhakar, P. K., & Doble, M. (2011). These are identified from number of cell culture for example *Coptis japonica* (Sato and Yamada, 1984; Barlaskar *et al.,* 2019), *Berberis spp.* and *Thalictrum spp*. The productivity of berberine was enhanced in the cell culture through enhancing the levels of phytohormones and nutrient in growth medium (Sato and Yamada, 1984; Feng *et al.,* 2019).

Elicitor to increase the production of Secondary Metabolite

Compound that stimulates each type of physiological abnormality of the plant is called Elicitors (Radman *et al.,* 2003). This explanation of elicitor includes both the compound that are released from the plant by action of the pathogen, these are called endogenous elicitor. And substance of pathogen origin is called exogenous elicitor. Elicitor can be used to raise secondary metabolite synthesis in the plant. They can play vital act in biosynthetic pathway to increase the production of the commercial vital compound. The secondary metabolites of plant are discharged due to defense response that activated and triggered through elicitor, the signal compound of defense response in the plant (Radman *et al.,* 2003).

Classification of Elicitors

Elicitor is divided into 2 class that is physical and chemical according to Radman *et al.* (2003). Elicitor is divided into 2 types as abiotic and biotic elicitors. Elicitors produced by biological agent are called as biotic elicitors. They are derived through the plant itself or from the pathogen. Elicitors not produced by biological agent are called as abiotic elicitors. They are classified in chemical compounds and physical factor.

Abiotic Elicitor

Abiotic elicitor is not having a biological origin. They are classified in chemical compounds and physical factor. For example: Metal ions (silver, europium, lanthanum, Cadmium, calcium), oxalate etc.

Biotic Elicitor

Biotic elicitors, they are having biological origin. They derive through the pathogen or by the plant itself. The first biotic elicitor was invented in 1968.

For example: Carbohydrates, fungus extract, yeast extract

- Polysaccharide: Alginate, Pectin, Chitosan (Nagpal *et al.,* 2013a; Nagpal *et al*., 2013b)
- Oligosaccharide: Guluronate, Mannan, Galacturonides Mannuronate.
- Peptides: Glutathione.

Plant hormone as Elicitor

There are distinct plant hormones that are acting as elicitor such as Jasmonic acid (JA) and Salicyclic acid (SA). In this SA is providing the resistance to pathogen such as fungal, viral and bacterial (Singh *et al.,* 2017). While JA regulates the octadecanoid pathway and consequently, protein synthesis. They can be applied from the outside to activate same metabolic change which provides resistance to pathogen (Sharma *et al.,* 2018; Chilakapati *et al.,* 2020). The biochemical pathway of JA and SA both are helpful in elicitation process in the plant (Angelova *et al.,* 2006).

Elicitors from Carbohydrates

There are various carbohydrates which are advantageous in the over production of secondary metabolite in the plant tissue culture. In cell culture of the tobacco, carbohydrate elicitor is activating the signal transfer with the help of H2O2 production and calcium influx (Negeral and Javelle, 1995, Modgil *et al.,* 2012).

Use of Elicitors

(1) Ecological safety, because this process is explained by the inauguration of endemic immune potential of gene.

(2) Protective effect.

(3) Presence of many defense systems in induced resistance.

(4) Inauguration of non specific resistance to many of fungi, bacteria, viruses etc.

Distinct Features of Elicitors

Elicitor concentration

Concentration of elicitor is playing a vital function in the elicitation process of plant. (Namdeo *et al.,* 2002; Kaur *et al.,* 2013) Explained more aggregation of ajmalicine in *C. roseus* culture when it is treated with various concentration of elicitor extracts of *A. Niger, F. Moniliforme* and *T. virid,*. Ajmalicine aggregation is more in the cell elicited by more concentration (five percent) of the elicitor extract as comparing to less concentration (0.5 percent) (Singh *et al.,* 2012). So, enhancing the concentration further upto 10 percent negatively damaged the aggregation of ajmalicine (Roewer *et al.,* 1992).

Duration of elicitor exposure

In an experiment, *C. roseus* was incubated with elicitor extract of the *A. Niger, T. viride* and *F. moniliforme* for 96 h, 72hour, 48h and 24h, respectively. Approximately amount of ajmalicine in *C. roseus* cells enhanced approximately 3 fold when incubated with extract of *T. viride* for 48 h, however 2 fold enhancement observed in the cell which is elicited with the *F. moniliforme* and *A. niger* (Namdeo *et al.,* 2002). Further enhancing exposure time results in reduction in ajmalicine content.

Age of culture

This is vital component in the bioactive compound production through elicitation. In previous study, through elicitation cells of *C. roseus* of twenty-day old culture was showing more yield of the ajmalicine (Namdeo *et al.,* 2002).

Nutrient composition

For elicitation process in plant, medium selection or composition of medium is also playing an important function. Accumulation in case of ajmalicine has been observed large in the Zenk's production medium. In Murashige and Skoog's medium the accumulation is less. So we can say that elicitation process is depend upon media selection. The elicitation process efficiency is depend upon presence of growth regulator in the media, nutrient composition of the medium, environmental condition,s elicitor specificity etc.

Out of these, method of elicitation is high economical beneficial in the plant tissue culture (Manorma *et al.,* 2011). Biochemistry and phytochemistry of elicitor are very helpful to increase the amount of secondary metabolite like flavonoids volatile oils, alkaloids, resins tannins etc. by plant cell (Namdeo *et al.,* 2004).

References

Amit, K.; Chiang, P.; & Chen, S. (2014). Interrelationship between secondary metabolites of cereals and agronomic practice. International Proceedings of Chemical, Biological and Environmental Engineering (IPCBEE), 79, 11-14.

Angelova, Z.; Georgiev, S and Roos, W (2006). Elicitation of plants. Biotechnology & Biotechnological Equipment, 20(2): 72-83.

Barlaskar, W. H.; Sharma, N. R.; Kumar, G.; & Kataria, S. (2017). Effect of Host Trees on Berberine Content in Stem of Tinospora cordifolia Climber: A Preliminary Study. Research Journal of Pharmacy and Technology, 10(3), 818-822.

Batra, P.; Naithani, R.; & Sharma, A. K. (2013). Flavonoids and their Therapeutic Potential as Anti Cancer Agents: Mechanism, Factors and Regulation. Frontiers in Anti-Cancer Drug Discovery, 2, 93.

Berli, F. J.; Moreno, D.; Piccolo, P.; Hespanhol-Viana, L.; Silva, M. F.; Bressan-Smith, R.; Cavarnaro, J. B. and Bottini, R (2010). Abscisis acid is involved in the response of grape (Vitis vinifera L.) cv. Malbec leaf tissues to ultraviolet-B radiation by enhancing ultraviolet- absobing compounds, antioxidant enzymes and membrane sterols. Plant Cell & Environment, 33(1): 1-10.

Bertin, C.; Yang, X. and Weston, L. A (2003). The role of root exudates and allelochemicals in the rhizospere. Plant and Soil, 256: 67-83.

Bhatt, S. M. (2012). Biotechnological approaches may alleviate lignin, a major toxicant released from paper industry. Journal of Bioremediation and Biodegradation, 3(9).

Brooker, N.; Windorski, J and Blumi, E (2008). Halogenated coumarins derivatives as novel seed protectants. Communication in Agriculture and Applied Biological Sciences, 73(2): 81-89.

Caldwell, M. M.; Robberechts, R and Flint, S. D (1983). Internal filters: prospects for UV-acclimation in higher plants. Physiologia Plantarum, 58: 445-450.

Chauhan, S.; Kaur, A.; Vyas, M.; & Khatik, G. L. (2017). Comparison of Antidiabetic and Antioxidant Activity of Wild And Cultivated Variety of Rauwolfia Serpentina. Asian J Pharm Clin Res, 10(12), 404-406.

Chilakapati, R.; Mannully, C. T.; Ghosh, M.; & Pulicherla, K. K. (2020). Characterization and Expression Profiling of Recombinant Parathyroid Hormone (rhPTH) Analog 1–34 in Escherichia coli, Precise with Enhanced Biological Activity. International Journal of Peptide Research and Therapeutics, 26(1), 93-105.

Crawford, N. M.; Kahn, M. L.; Leustek, T and Long, S. R (2000). Nitrogen and sulfur. In Biochemistry and Molecular Biology of Plants, Buchanan BB, Gruissem W, Jones RL, eds, (Rockville, MD: American Society of Plant Biologists), 824–849.

Dakora, F. D and Phillips, D. A (2002). Root exudates as mediators of mineral aquisation in low nutrient environments. Plant and Soil, 245: 35-47.

Dipika, M.; Gharde, S. K.; Datta, S.; Singh, S. K.; Savita, R. T.; & Kaur, P. (2018). Disease Resistance In Leguminous Vegetables. Annals Of Biology, 34(2), 235-239.

Eisner, T and Meinwald, J (1995). Chemical ecology: The chemistry of biotic interaction. Eds, National Academy Press, Washington, DC.

Feng, X.; Sureda, A.; Jafari, S.; Memariani, Z.; Tewari, D.; Annunziata, G.; ... & Sychrova, A. (2019). Berberine in cardiovascular and metabolic diseases: from mechanismsto therapeutics. Theranostics, 9(7), 1923.

Fraga, B. M (1988). Natural sesquiterpenoids. Natural Product Reports, 5: 497-521.

Gershenzon, J.; Croteau, R and Terpenoids (1991). In Herbivores their interaction with secondary plant metabolites. Vol I: The chemical participants, 2nd ed.; G.A. Rosenthal and M.R. Berenbaum, eds, Academic press, San Diego, 165-219.

Gould, J. M (1983). Probing the structure and dynamics of lignin in situ. What's New in Plant Physiology, 14: 25-91.

Guggenheim, M (1913). Dioxyphenylalanin, eine neue Aminosaure aus Vinca faba. Z. Physiol. Chem, 88: 276.

Gupta, K.; Garg, S.; Singh, J.; & Kumar, M. (2014). Enhanced production of napthoquinone metabolite (shikonin) from cell suspension culture of Arnebia sp. and its up-scaling through bioreactor. 3 Biotech, 4(3), 263-273.

Gupta, M.; Gupta, A.; & Gupta, S. (2013). Insecticidal Activity of Essential Oils Obtained from Piper nigrum and Psoralea corylifolia Seeds against Agricultural Pests. Asian Journal of Research in Chemistry, 6(4), 360-363.

Gupta, M.; Gupta, A.; & Gupta, S. (2014). Characterization of Secondary Metabolites via LC-MS Analysis of DCM Extracts of Solanum nigrum. Biosci Biotechnol Res Asia. Vol. 11(2), 531-535

Hadacek, F (2002). Secondary Metabolites as Plant Traits: Current Assessment and Future Prospective. Critical Reviews in Plant Sciences, 21: 273-322.

Handa, N.; Kohli, S. K.; Sharma, A.; Thukral, A. K.; Bhardwaj, R.; Abd-Allah, E. F. & Ahmad, P. (2019). Selenium modulates dynamics of antioxidative defence expression, photosynthetic attributes and secondary metabolites to mitigate chromium toxicity in Brassica juncea L. plants. Environmental and Experimental Botany, 161, 180-192.

Harborne, J. B (1988). The comparative biochemistry of Phytoalexin Induction in Plants. Biochemical Systematics and Ecology, 27: 335-367.

Hegnauer, R (1988). Biochemistry, distribution and taxonomic relevance of higher plant alkaloids. Phytochemistry, 27: 2423-2427.

Hell, R (1997). Molecular physiology of plant sulfur metabolism. Planta, 202: 138-148.

Irving, H. R.; Gehring, C. A. and Parish, R. W (1992). Changes in cytosolic pH and calcium of guard cells precede stomatal movements. Proceedings of the National Academy of Sciences of the USA, 89: 1790-1794.

Jagendorf, A. T (1967). Acid base transition and photophosphorylation by chloroplast. Federation Proceedings, 26: 1361-1369.

Jordon, M. A and Wilson, L (1995). Microtuble polymerization dynamics, mitotic, and cell death by paclitaxel at low concentration. American Chemical Society Symposium Series, 583: 138-153.

Kang, S. Y and Kim, Y. C (2007). Decursinol and decursin protect primary cultured rat cortical cells from glutamate-induced neurotoxicity. Journal of Pharmacy and Pharmacology, 59(6): 863-870.

Kaur, S.; Kaur, J.; & Pankaj, P. P. (2014). Isolation and characterization of antibiotic producing microorganisms from soil samples of certain area of Punjab region of India. International Journal of Pharmaceutical and Clinical Research, 6(4), 312-315.

Kesarwani, A.; Chiang, P. Y.; Chen, S. S.; & Su, P. C. (2013). Antioxidant activity and total phenolic content of organically and conventionally grown rice cultivars under varying seasons. Journal of Food Biochemistry, 37(6), 661-668.

Knaff, D. B (1991). Regulatory phosphorylation of chloroplast antenna proteins. Trends Biochemical Sciences, 16: 82-83.

Kondo, T.; Yoshida, K.; Nakagawa, A.; Kawai, T.; Tamura, H and Goto, T (1992). Structural basis of blue- color development in flower petals from commelina communis. Nature, 358: 515-518.

Lake, J. A.; Field, K. J.; Davey, M. P.; Beerling, D. J and Lomax, B. H (2009). Metabolomic and physiological responses reveal multi-phasic acclimation of Arabidopsis thaliana to chronic UV radiation. Plant, cell & environment, 32(10): 1377-1389.

Leustek, T (2002). Sulfate metabolism. Somerville CR, Meyerowitz EM, eds, The Arabidopsis Book. American Society of Plant Biologists, Rockville, MD. doi/10.1199/tab.0009.

Lewis, N. G. and Yamamoto, E (1990). Lignin: Occurrence, biogenesis and biodegradation. Annual Review of Plant Physiolgy and Plant Molecular Biology, 41: 455-496.

Lewis, W. H. and Elvin-Lewis, M. P. F (1977). Medical Botany; plants affecting man's health. Wiley, New York.

Manorma, Sharma.; Archana, Sharma.; Ashwani, Kumar and Saikat, Kumar. Basu (2011). Enhancement of secondary Metabolites in Cultured Plant Cells through Stress Stimulus. American Journal of Plant Physiology 6(2): 50□71.

Marx, J (2004). The roots of plant-microbe collaborations. Science, 304: 234-236.

Mccarty, D.; Hattori, T.; Carson, C.B.; Vasil, V.; Lazar, M and Vasil, I.K (1991). The vivporous-1 development gene of maize encodes a novel transcription activator. Cell, 66: 895-905.

Modgil, R.; Mankotia, K.; Gupta, R.; Malhotra, S. R.; & Tanwar, B. (2012). Carbohydrates, minerals, antinutritional constituents and In vivo protein quality of domestically processed cow peas,(Vigna Ungiculata). Legume Research-An International Journal, 35(3), 214-219.

Nagpal, K.; Singh, S. K.; & Mishra, D. (2013b). Evaluation of safety and efficacy of brain targeted chitosan nanoparticles of minocycline. International journal of biological macromolecules, 59, 20-28.

Nagpal, K.; Singh, S.K.; & Mishra, D.N. (2013a). Formulation, optimization, in vivo pharmacokinetic, behavioral and biochemical estimations of minocycline loaded chitosan nanoparticles for enhanced brain uptake. Chemical and Pharmaceutical Bulletin, 61(3), 258-272.

Namdeo (2004). Investigation on pilot scale bioreactor with reference to the synthesis of bioactive compounds from cell suspension cultures of Catharanthus roseus Linn. Ph.D. Thesis, Devi Ahilya Vishwavidyalaya, Indore, M.P. India.

Namdeo, S.; Patil, D. P and Fulzele (2002). Influence of fungal elicitors on production of ajmilicine by cell culture of Catharanthus roseus. Biotechnol Prog, 18: 159-162.

Negeral, F and Javelle (1995). Induction of phenyl propanoid and tyramine metabolism in pectinase or pronase elicited cell suspension culture of tobacco. Physiol Plant, 95: 569□ 574.

Osbourn, A.; Qi, E.; Townsend, B. and Qin, B (2003). Bisecting Plant Secondary Metabolism– Constitutive Chemical Defenses in Cereals. New Phytol, 159: 101-108.

Pearce, G.; Strydom, D.; Johnson, S and Ryan, C. A (1991). A polypeptide from tomato leaves induces wound inducible protienase inhibitor proteins. Science, 253: 895-898.

Phillipson, J. D (1990). Plants as source of valuable products. In B.V. Charlwood, and M.J.C. Rhodes (eds.), Secondary Prod- ucts from Plant Tissue Culture. Oxford: Clarendon Press, 1-21.

Picman, A. K (1986). Biological activities of sesquiterpene lactones. Biochemical systematics and Ecology, 14: 255-281.

Prabhakar, P. K.; & Doble, M. (2011). Effect of natural products on commercial oral antidiabetic drugs in enhancing 2-deoxyglucose uptake by 3T3-L1

adipocytes. Therapeutic advances in endocrinology and metabolism, 2(3), 103-114.

Prabhakar, P. K.; Prasad, R.; Ali, S.; & Doble, M. (2013). Synergistic interaction of ferulic acid with commercial hypoglycemic drugs in streptozotocin induced diabetic rats. Phytomedicine, 20(6), 488-494.

Prasad, D. (2010). Phenolic Glycoside from root of Viburnum cylindricum. Biosciences, Biotechnology Research Asia Vol. 7(1), 501-502.

Rabea, E. L.; Badawy, M. E. T.; Stevens, C. V.; Smagghe, G and Steurbaut, W (2003). Chitosan as Antimicrobial Agent: Applications and Mode of Action. Biomacromolecules, 4(6): 1457-1465.

Radman, R.; Sacz, T.; Bucke, C.; Keshvartz, T. (2003). Elicitation of plants and microbial cell systems. Biotehnol. Appl. Biochem.; 37: 91□102.

Ravishankar, G. A.; Sarma, K. S.; Venkataraman, L. V and Kadyan A. K (1988). Effect of nutritional stress on capsaicin pro- duction in immobilized cell cultures of Capsicum annuum. Current Science, 57: 381-383.

Rice and Elroyleon (1984). Allelopathy, (1st edition, November 1974) 2nd edition. Academic Press, 422.

Roewer, N.; Cloutier and R Van der Heijden (1992). Transient induction of tryptophan decarboxylase (TDC) and strictosidine synthase, (SS) genes in cell suspension cultures of Catharanthus roseus. Plant Cell Rep, 11(2): 86□89.

Roze, L. V.; Chanda, A and Linz, J. E (2011). Compartmentalization and molecular traffic in secondary metabolism: a new undestanding of established cellular processes. Fungal Genetics and Biology, 48: 35–48.

Sato, F and Yamada, Y (1984). High berberine producing cul- tures of Coptis japonica cells. Phytochemistry, 23: 281-285.

Savirnata, N. M.; Jukunen-Titto, R.; Oksanen, E and karjalainen, R. O (2010). Leaf phenolic compounds in red clover (Trfolium Pratense L.) induced by exposure to moderately elevated ozone. Environmental Pollution, 158(2): 440-446.

Seigler, D. S (1981). Secondery metabolites and plant systematic. Conn EE (ed), The biochemistry of plants, Vol 7. Secondery plant products. Plenum, New York and London, 139-176.

Sharma, A.; Devi, Savita A.; Singh, Kamaldeep.; & Prabhakar, P. K. (2018). Correlation of body mass index with thyroid-stimulating hormones in thyroid patient. Asian J. Pharm. Clin. Res, 11, 65-68.

Sharma, S.; & Parihar, L. (2014). Effect of Mobile Phone Radiation on Nodule Formation in the Leguminous Plants. Current World Environment, 9(1), 145.

Singh, A.; Lin, Y.; Liu, W.; Pan, J.; Ren, C.; Zeng, D.; & Yu, S. (2014). Berberine as an effective corrosion inhibitor for 7075 aluminium alloy in 3.5% NaCl solution. Int. J. Electrochem. Sci, 9, 5164-5176.

Singh, D.; Raina, T. K.; Kumar, A.; Singh, J.; & Prasad, R. (2019). Plant microbiome: A reservoir of novel genes and metabolites. Plant gene, 18, 100177.

Singh, J.; Mirza, A.; Singh, S.; & Singh, P. (2017). Impact of phytohormones on physio-chemical properties of tropical and subtropical fruits: a review. Plant Archives, 18(1), 12-18.

Singh, S.; Agarwal, R. K.; Tiwari, S. C.; & Singh, H. (2012). Antibiotic resistance pattern among the Salmonella isolated from human, animal and meat in India. Tropical animal health and production, 44(3), 665-674.

Singh, S.; Bhatia, S.; & Prasad, S. B. (2016). In silico Identification of Polyphenolic Compounds from the Grape fruit as Quorum sensing inhibitors. Journal of Chemical and Pharmaceutical Research, 8(5), 411-419.

Sirohi, S. K.; Goel, N.; & Singh, N. (2014). Utilization of saponins, a plant secondary metabolite in enteric methane mitigation and rumen modulation. Annual Research & Review in Biology, 1-19.

Stamp and Nancy (2003). Out of the Quagmire of plant defense hypothesis. The Quarterly Review of Biology, 78(1): 23-55.

Staskawicz, B. J.; Ausubel, F. M.; Baker, B. J.; Ellis, J. G and Jones, J. D (1991). Molecular genetics of plant disease resistance Science. Science, 268: 661□667.

Steegh, M.; Bais, H. P.; de Gouw, J.; Goldan, P.; Kuster, W.; Northway, M.; Fall, R and Vivanco, J. M (2004). Proton-transfer-reaction mass spectrometry (PTR-MS) as a new tool for real time analysis of root-secreted Volatile Organic Compounds (VOC) in Arabidopsis thaliana. Plant Physiology, 135: 47-58.

Suffness, M (1995). Taxol: Science and Applications. CRC Press, Boca Raton, FL.

Taiz, L and Zeiger, E (1995). Plant Physiology Edition. Panima Publishing Corporation, New Delhi.

Tam, W. H. J.; Constabel, F and Kurz, W. G. W (1980). Codeine from cell suspension cultures of Papaver somniferum. Phytochemistry 19: 486-487.

Tang, W and Eisenbrand, G (1992). Panax ginseng C.A. Mayer. Chinese drugs of plant origin. Springer, Berlin, 710-773.

Tanwar, B.; & Modgil, R. (2012). Flavonoids: Dietary occurrence and health benefits. Spatula Dd, 2(1), 59-68.

Turlings, T.C.J.; Loughrin, J.H.; Mccall, P.J.; Roese, U.S.R.; Lewis, W.J. and Tumlinson, J.H. (1995). How caterpillar- damaged plants protect themselves by attracting parasitic wasps. Proceeding of the National Academy of Sciences of the USA, 92: 4169-4174.

Wang, J.W. and Wu, J.Y. (2013). Effective elicitors and process strategies for enhancement of secondary metabolite production in hairy root cultures. Adv Biochem Eng Biotechnol, 134: 55-89.

Yoshikawa, T and Furuya, T (1985). Morphinan alkaloid pro- duction by tissues differentiated from cultured cells of Pa- paver somniferum. Planta Med, 2: 110-113.