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Plant growth regulator mediated consequences of secondary metabolites in medicinal plants

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ABSTRACT

Secondary metabolites not only play vital role in plant defense against herbivory and other interspecies defenses but also used by humans as medicines, flavorings, pharmaceuticals, agrochemicals, fragrances, colours, biopesticides, food additives and drugs. Many of the drugs retailed today are simple synthetic modifications of the naturally obtained substances. The developing commercial status of secondary metabolites in recent years has resulted in a great interest in secondary metabolism. Different strategies have been extensively studied with the objective of improving the production of secondary metabolites in plants. Based on this limelight, the focus of the present review is to study the application of plant growth regulators for the production of some essential plant secondary metabolites. This review covers brief introduction of secondary metabolites and plant growth regulators and production of secondary metabolites by using different plant growth regulators according to their classification.

1. Introduction

Plants face a number of opponents in natural systems and therefore possess innumerable defense and have evolved multiple resistance mechanisms through which they are capable to cope with various kinds of biotic and abiotic stress (Ballhorn et al., 2009). Plants defend themselves by producing some compounds of diverse chemical nature called as secondary metabolites. Plant secondary metabolites are recognized as compounds that are essential for the plant acclimatization and defense but have no vital role in the continuation of life processes in the plants. It is believed that most of the 100,000 known secondary metabolites are to be involved in plant chemical defense systems, which are made throughout millions of ages during which plants have co-existed with their invaders (Wink, 1999). Secondary metabolites are significant source of pharmaceuticals as well as play a dynamic role in the adaptation of plants to their environment (Rao and Ravishankar, 2002).

Secondary metabolites are responsible for the medicinal value of the plants but they have very limited distribution than primary metabolites. Research on plant secondary metabolites has increased during last 50 years due to value necessity of the daily lives including health care on these plant products (Mulabagal and Tsay, 2004). Many of these molecules are found in ppm levels in nature thus requires immense harvesting to attain adequate amounts of the drug. Therefore it is required to use eco-friendly system to achieve complex chemical structures biosynthesized by rare or endangered plant species that oppose domestication and the plants having slow growth rate (e.g., *Taxus* trees reach a peak production of taxol only after 60 years of growth). Cultivation of medicinal plants and in vitro production of plant secondary metabolites are the only sustainable ways to achieve the market demand. Accumulation of secondary metabolites normally occurs in plants introduced to various signal molecules or elicitors.

Plant growth regulators (PGRs) have been used as proficient elicitors to stimulate production of plant secondary metabolites. Plant growth regulators include hormonal substances of natural occurrence (phytohormones) as well their synthetic analogues (Basra, 2000) (Table 1). The concept of phytohormone was recommended at the end of 19th Century by Julian von Sachs, who described them as mobile endogenous compounds (Spartz and Gray, 2008). Plant growth regulators are simple molecules that have specific effects on plant growth and are effective even in low concentrations (Nambara and Marion-Poll, 2005; Teale et al., 2006). Traditionally, synthetic plant growth regulators are used as precious research tools to elucidate physiological responses of plants or to explore biochemical control mechanisms. Since 1940, natural as well as synthetic growth regulators have been used in agriculture to control developmental processes like germination, growth, vegetative reproduction, maturation, senescence and post-harvest (Basra, 2000). PGRs not only control antioxidant potential, fundamental growth and developmental processes but are also known to regulate plant secondary metabolites production in plant tissue culture (Dörnenburg and Knorr, 1995). According to Zhao et al. (2005),

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Table 1
Major hormones and their types.

Major hormones	Natural hormones	Synthetic hormones
Auxin	Indole-3-acetic acid (IAA)	Indole 3 butyric acid (IBA)
	Indole-3-acetonitrile (IAN)	Indole 3 propionic acid (IPA)
	Indole-3-acetaldehyde (IAc)	Indazole 3 acetic acid
	Ethylindoleacetate	Chlorophenoxypropionic acids
	Indole-3- pyruvic acid (IPyA)	Naphthalene acetic acid (NAA)
		Phenoxy acetic acid (PAA)
		2, 4-dichlorophenoxy acetic acid (2, 4-D)
		2,4,5- trichlorophenoxy acetic acid (2,4,5-T)
		Naphthalene acetamide (NAAM)
		2-napthoxyacetic acid (NOA)
		2, 3,5-Triodobenzoic acid (TIBA)
		Thianaphthen-3-propionic acid (IPA)
Cytokinin	Ribosylzeatin	6-Benzyl amino purine
	Zeatin	6-Phenyl amino purine
	Isopentinyladenine	Kinetin
	Dihydrozeatin	[(N-Benzyl-9-(2-etrahydropyranyl) adenine] (PBA)
		Diphenylurea
		Thidiazuron
		Benzimidazole
		Adenine
		6-(2-Thenylamino) purine
Gibberellins	GA	GA
	GA4	GA_3
	GA7	
Ethylene	Ethylene	Ethephon
		Ethrel
Brassinosteroids	Dolicholide	Five 5-hydroxy-6-ketone
	28-homodolicholide	
	Castasterone	
	Dolichosterone	
	28-homodolichosterone	
	Typhasterol	
Jasmonates	Jasmonic acid	Methyl dihydrojasmonate
		Di hydrojasmonic acid
		Methyl jasmonate
Strigolactones	Strigol	GR24
	orobanchol	

PGRs are active at low concentrations, have specific effects on growth and development and are involved in plant secondary metabolism.

2. Influence on secondary metabolites

The plant reaction to plant growth regulators may differ with species, age of plant, varieties, environmental conditions, stage of development, physiological and nutritional status and endogenous hormonal balance (Aftab et al., 2010; Idrees et al., 2010a, 2010b, 2011, 2012; Naeem et al., 2009, 2010, 2011). A number of studies have been performed and confirmed in vast plants to find out the effects of unlike plant growth regulators on secondary metabolite production (Weathers et al., 2005; Rojbayani, 2007; Khan et al., 2008; Shilpashree and Rai, 2009).

Azeez and Ibrahim (2014) revealed that presence of active compounds in cultured cells at higher levels through optimization of cultural conditions may be due to PGRs, added to the medium for initiation of callus of *Hypericum triquetrifolium*. Increase in production of secondary metabolites is due to cell multiplication and division caused by PGRs (Staba, 1980). Since PGRs have significant effects on the metabolism of secondary metabolites, they are effective to stimulate secondary metabolite production in *Saintpaulia ionantha* (Al-Sane et al., 2010) and *Hypericum mysorense* (Shilpashree and Rai, 2009). According to Duangporn and Siripong (2009) naphthalene acetic acid (NAA) and benzyl adenine (BA) increased secondary product accumulation in callus cultures of *Phyllanthus acidus*. It was observed that production of secondary metabolite in tissue culture was improved with indole acetic acid (IAA) and naphthalene acetic acid in *Coscinium fenestratum* (Nair et al., 1992) or else by 2,4-dichlorophenoxyacetic acid (2, 4-D) in *Nicotiana tabacum* (Ikeda et al., 1976).

When adventitious roots were treated with KIN (kinetin) and IBA (indole 3 butyric acid) in combination with thidiazuron (TDZ), fresh weight (FW) and dry weight (DW) reduced but secondary metabolite content increased in *Morinda citrifolia* and the secondary metabolite content was (including 1, 1-diphenyl-2-picrylhydrazyl activity) higher in TDZ (thidiazuron) treated than in kinetin-treated roots (Baque et al., 2010). Differences in cytokinin concentrations even in combination with NAA (equimolar concentrations) considerably affected secondary metabolite production in some cases in *Aloe arborescens* (Amoo et al., 2012). Sakakibara et al. (2006) observed that cytokinins significantly suppress some transporters of macronutrients such as nitrate, sulphate, ammonium and phosphate on one hand and nitrate on the other side normalizes the genes expression involved in secondary metabolite pathways. Rawat et al. (2013) reported that 6-benzyl amino purine (BAP) was found to be more efficient in improving shoot regeneration and production of secondary metabolite in *Aconitum violaceum* compared to thidiazuron and differences in concentrations of cytokinins significantly enhanced secondary metabolite production in some cases.

Cytokinins have enhancing effect on the secondary metabolites in *Hypericum sampsonii* and *Hypericum perforatum* plantlets (Liu et al., 2007). Kalt et al. (2001) observed that ABA (abscisic acid) application caused oxidative stress in *Orthosiphon stimaneus* and at the same time stimulated the secondary metabolites production. Gibberellic acid (GA_3) has also been shown to stimulate the growth of hairy roots in numerous species with a variable amount of secondary metabolite production in *Chicorium intybus* (Bais et al., 2001). Although salicylic acid (SA), methyl jasmonate and jasmonate (JA) may trigger plant secondary metabolite biosynthesis through distinct signaling pathways (Zhao et al., 2005), they are all act together with NO (nitric oxide) in facilitating plant secondary metabolite production. NO has been reported to play significant roles in elicitor-induced secondary metabolite production in tissue and cell cultures of medicinal plants (Zhang et al., 2012). The NO production in *Taxus chinensis* cells increased with the MeJA treatment, suggesting a dose-dependent stimulation by MeJA (Wang and Wu, 2005). When MeJa was applied exogenously to plant cell cultures of a variety of species it stimulated the operation of secondary biosynthetic pathways and led to increased production of miscellaneous plant secondary metabolites, including terpenoids, alkaloids, flavonoids and phenylpropanoids (Uppalapati et al., 2005; Rischer et al., 2006; Wasternack and Hause, 2013). CA (Caffeic Acid) and MeJA applications considerably enhanced secondary metabolite production in *Rubia tinctorum* root cultures (Bicer et al., 2017).

There are three foremost groups of secondary metabolites i.e., terpenes, phenolics and nitrogen, sulphur comprising compounds (Fig. 1). Terpenes are composed of 5-C isopentanoid units. Phenolics synthesized principally from products of the shikimic acid pathway. Members of the third major group i.e., nitrogen, sulphur comprising compounds are synthesized largely from common amino acids (Van Etten et al., 2001). They have a much delimited distribution than primary metabolites in the entire plant kingdom i.e., they are frequently found only in one plant species or a taxonomically related group of species.

2.1. Terpenes

Terpenes signify one of the most largest and diverse classes of secondary metabolites (Table 2) and are linked by their communal biosynthetic source from acetyl-coA or else glycolytic intermediates (Grayson, 1998). Majority of the different terpenes structures produced by plants as secondary metabolites are supposed to be intricate in