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The regulatory mechanism of fungal elicitor-induced secondary metabolite biosynthesis in medical plants.

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Table1. The fungal elicitors and their effects on secondary metabolites accumulation in medical plants

Plants	cultured system	secondary metabolites	Types of secondary metabolites	Fungal	Fungal elicitors	Types of fungal elicitors	Folds(Compared with the control group)	Reference
<i>Artemisia annua</i> L.	hairy root culture	sesquiterpene lactone	artemisinin	<i>Piriformospora indica</i>	fungal extract	fungal extract	2.44 fold	(Ahlawat <i>et al.</i> 2014)
<i>Nicotiana tabacum</i>	cell culture	capsidiol	Sesquiterpene	<i>Trichoderma viride</i>	cellulase	cellulase	23 fold	(Mandujano-Chavez <i>et al.</i> 2000)
<i>Artemisia annua</i> L.	hairy root cultures	artemisinin	sesquiterpene lactone	<i>Penicillium chysogenum</i> 3446	mycelial extracts	fungal extract	1.33 fold	(Liu <i>et al.</i> 1999)
<i>Artemisia annua</i> L.	hairy root cultures	artemisinin	sesquiterpene lactone	<i>Colletotrichum gloeosporioides</i>	crude cell-wall extract	fungal extract	1.5 fold	(Wang <i>et al.</i> 2006)
<i>Artemisia annua</i> L.	hairy root cultures	artemisinin	sesquiterpene lactone	<i>Colletotrichum</i> sp.	mycelial extracts	fungal extract	1.44 fold	(Wang <i>et al.</i> 2001)
<i>Atractylodes lancea</i>	plantlet	atractylone		<i>Gilmaniella</i> sp.	fungal extract	fungal extract	2 fold	(Wang <i>et al.</i> 2012)
<i>Brugmansia candida</i>	hairy root culture	scopolamine	tropane alkaloids	yeast	yeast extract:	fungal extract	7 fold	(Pitta–Alvarez <i>et al.</i> 2000)
<i>Catharanthus roseus</i>	cell culture	catharanthine	indole alkaloid	<i>Pythium vexans</i>	mycelial extracts	fungal extract	6.8 fold	(Nef <i>et al.</i> 1991)
<i>Catharanthus roseus</i>	cell culture	ajmalicine	indole alkaloid	<i>Fusarium solani</i> ,	mycelial homogeneate	fungal extract	2.5-3.3 fold	(Zhao <i>et al.</i> 2001)
<i>Catharanthus roseus</i>	cell culture	serpentine	indole alkaloid	<i>Absidia cristata</i>	mycelial homogeneate	fungal extract	1.2-1.6 fold	(Zhao <i>et al.</i> 2001)

<i>Catharanthus roseus</i>	cell culture	ajmalicine	indole alkaloid	<i>Penicillium spimulorum</i>	mycelial homogeneate	fungals extract	2.5-3.3 fold	(Zhao <i>et al.</i> 2001)
<i>Catharanthus roseus</i>	cell culture	ajmalicine	indole alkaloid	<i>Verticillium dahliae</i> ,	mycelial homogeneate	fungals extract	2.5-3.3fold	(Zhao <i>et al.</i> 2001)
<i>Catharanthus roseus</i>	cell culture	ajmalicine	indole alkaloid	<i>Pythium irregulare</i> ,	mycelial homogeneate	fungals extract	2.5-3.3fold	(Zhao <i>et al.</i> 2001)
<i>Catharanthus roseus</i>	cell culture	ajmalicine	indole alkaloid	<i>Ustilaginodia verens</i>	mycelial homogeneate	fungals extract	2.5-3.3 fold	(Zhao <i>et al.</i> 2001)
<i>Catharanthus roseus</i>	cell culture	serpentine	indole alkaloid	<i>Fusarium solani</i> ,	mycelial homogeneate	fungals extract	1.2-1.6 fold	(Zhao <i>et al.</i> 2001)
<i>Catharanthus roseus</i>	cell culture	serpentine	indole alkaloid	<i>Pythium irregulare</i> ,	mycelial homogeneate	fungals extract	1.2-1.6 fold	(Zhao <i>et al.</i> 2001)
<i>Catharanthus roseus</i>	cell culture	catharanthine	indole alkaloid	<i>Fusarium solani</i> ,	mycelial homogeneate	fungals extract	4-6.6 fold	(Zhao <i>et al.</i> 2001)
<i>Catharanthus roseus</i>	cell culture	catharanthine	indole alkaloid	<i>Pythium irregulare</i> ,	mycelial homogeneate	fungals extract	4-6.6 fold	(Zhao <i>et al.</i> 2001)
<i>Catharanthus roseus</i>	cell culture	catharanthine	indole alkaloid	<i>Absidia cristata</i>	mycelial homogeneate	fungals extract	4-6.6 fold	(Zhao <i>et al.</i> 2001)

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<i>Catharanthus roseus</i>	cell culture	catharanthine	indole alkaloid	<i>Aspergillum niger</i> ,	mycelial homogeneate	mycelial homogeneate	4-6.6 fold	(Zhao <i>et al.</i> 2001)	
<i>Catharanthus roseus</i>	cell culture	catharanthine	indole alkaloid	<i>Ustilaginodia verens</i>	mycelial homogeneate	mycelial homogeneate	4-6.6 fold	(Zhao <i>et al.</i> 2001)	
<i>Catharanthus roseus</i>	cell culture	ajmalicine	indole alkaloid	<i>Aspergillus niger</i> , <i>Fusarium moniliforme</i> and .	cell wall	cell wall	2 fold	(Namdeo <i>et al.</i> 2002)	
<i>Catharanthus roseus</i>	cell culture	ajmalicine	indole alkaloid	<i>Trichoderma viride</i>	cell wall	cell wall	3 fold	(Namdeo <i>et al.</i> 2002)	
<i>Centella asiatica</i> L.	cell culture	asiaticoside	saponin	yeast	yeast extract	fungal extract	1.4 fold	(Kim <i>et al.</i> 2004)	
<i>Cichorium intybus</i> L.	hairy root cultures	coumarin	coumarin	<i>Phyophthora parasitica</i>	media titrate	fungal extract	1.3 fold	(Bais <i>et al.</i> 2000)	
<i>Cinchona robusta</i> How.	cell culture	anthraquinone	anthraquinone	<i>Phytophthora cinnamomi</i>	mycelial homogeneate	mycelial homogeneate	4 fold	(Ramos-Valdivia <i>et al.</i> 1997)	
<i>Coleus blumei</i>	cell culture	rosmarinic acid	alcohol glycoside	<i>Pythium aphanidermatum</i>	glucose equivalent	fungal extract	2 fold	(Szabo <i>et al.</i> 1999)	
<i>Cupressus lusitanica</i>	cell culture	β -thujaplicin		fungal elicitor and ferrous ion			3-4 fold	(Zhao <i>et al.</i> 2001)	
<i>Daucus carota</i> L.	cell culture	p-hydroxybenzoic acid		<i>Pythium aphanidermatum</i> (Edson) Fitzp.	mycelial homogeneate	mycelial homogeneate	2.5 fold	(Schnitzler <i>et al.</i> 1992)	
<i>Daucus</i>	callus	anthocyanin	flavonoids	<i>Aspergillus</i>	mycelial	mycelial	1.25 fold	(Rajendran <i>et al.</i> 1994)	

<i>carota</i> L.	cultures			<i>flavus</i>	extract	extract		
<i>Dioscorea galeottiana</i>	cell culture	diosgenin	Saponin	<i>Alternaria tenuis</i>	fungals extract	fungals extract	1.2 fold	(Rojas <i>et al.</i> 1999)
<i>Euphorbia pekinensis</i>	cell culture	isoeuphpeki nensin/euphol	terpenoid	<i>Fusarium</i> sp.	fungals extract	fungals extract	5.81 fold/3.56 fold	(Gao <i>et al.</i> 2011)
<i>Hyoscyamus muticus</i>	root culture	lubimin	sesquiterpene	<i>Rhizoctonia solani</i>	crude cell wall	cell wall	4 fold (compared with MeJa-induced group)	(Singh <i>et al.</i> 1998)
<i>Hypericum perforatum</i> L	shoot organ culture	hypericin	glycoside	yeast	mannan	fungals extract	2 fold	(Kirakosyan <i>et al.</i> 2000)
<i>Hypericum perforatum</i> L	shoot organ culture	pseudohypericin	anthraquinone	yeast	mannan	fungals extract	4 fold	(Kirakosyan <i>et al.</i> 2000)
<i>Hypericum perforatum</i> L	cell culture	phenolic compounds	flavonoids	<i>Colletotrichum gloeosporioides</i>	fungals extract	fungals extract	2.7 fold	(Conceiçao <i>et al.</i> 2006)
<i>Linum album</i>	root culture	lignan	lignan	<i>Fusarium graminearum</i>	fungals extract	fungals extract	2-3 fold	(Bahabadi <i>et al.</i> 2014)
<i>Linum album</i>	root culture	lignan	lignan	<i>Trichoderma viride</i>	fungals extract	fungals extract	2.4 fold	(Bahabadi <i>et al.</i> 2014)
<i>Linum album</i>	root culture	lignan	lignan	<i>Sclerotinia sclerotiorum</i>	fungals extract	fungals extract	2 fold	(Bahabadi <i>et al.</i> 2014)
<i>Lithospermum</i>	cell culture	Shikonin	Naphthoquinones	<i>Penicillium species</i>	cell powder	cell powder	65 fold	(Kim <i>et al.</i> 1990)

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<i>Nicotiana tabacum</i>	cell culture	capsidiol	sesquiterpene	<i>Trichoderma viride</i>	celluase	celluase	5 fold	(Mandujano-Chavez <i>et al.</i> 2000)
<i>Panax ginseng</i>	cell culture	saponin	saponin	yeast	yeast extract	fungals extract	28 fold	(Lu <i>et al.</i> 2001)
<i>Panax ginseng</i> C.A. Meyer	hairy root culture	ginseng saponin	saponin	yeast	yeast extracts	fungals extract	1.17 fold	(Jeong <i>et al.</i> 2005)
<i>Piqueria trinervia</i>	cell culture	antifungal monoterpene	monoterpene	<i>Alternaria alternata</i> , <i>Fusarium poae</i> , <i>Phaecilomyces elegans</i>	fungals strains	fungals strains	/	(Saad <i>et al.</i> 2000)
<i>Polygonum tinctorium</i>	cell culture	indirubin	indole alkaloid	<i>Rhizoctonia solani</i>	cell wall	cell wall	1.43 fold	(Mareroa <i>et al.</i> 1997)
<i>Psoralea corylifolia</i> L.	cell culture	psoralen	furocoumarine	<i>Aspergillus niger</i>	fungals extract	fungals extract	9-fold	(Ahmed <i>et al.</i> 2014)
<i>Psoralea corylifolia</i> L.	cell culture	psoralen	furocoumarine	<i>Penicillium notatum</i>	fungals extract	fungals extract	4-7 fold	(Ahmed <i>et al.</i> 2014)
<i>Rubia tinctorum</i> L.	cell culture	anthraquinone derivatives	anthraquinone	<i>Botrytis cinerea</i>	fungals polysaccharide	polysaccharide	/	(Orbán <i>et al.</i> 2008)
<i>Scutellaria baicalensis</i>	cell culture	triterpenoids	terpenoids	yeast	yeast extract	fungals extract	2.8 fold	(Yoon <i>et al.</i> 2000)
<i>Solanum tuberosum</i>	hairy root cultures	antimicrobials	sesquiterpenes	<i>Agrobacterium rhizogenes</i>	mycelial homogenate	mycelial homogenate	2 fold	(Komaraiah <i>et al.</i> 2003)

<i>Solanum tuberosum</i> L.	cell culture	isoprenoid	sesquiterpenoid	<i>Phytophthora infestans</i>	arachidonic acid	arachidonic acid	/	(Choi <i>et al.</i> 1994)
<i>Salvia miltiorrhiza</i> Bge.	hairy root culture	tanshinone	diterpene	<i>Trichoderma atroviride</i>	hyphae	hyphae	21.1 fold	(Ming <i>et al.</i> 2012)
<i>Taverniera cuneifolia</i> (Roth) Arn.	root culture	saponin	glycyrrhizic acid	<i>Aspergillus niger</i>	hyphae	hyphae	2 fold	(Awad <i>et al.</i> 2014)
<i>Taverniera cuneifolia</i> (Roth) Arn.	root culture	saponin	glycyrrhizic acid	<i>Aspergillus tenuis</i>	hyphae	hyphae	1 fold	(Awad <i>et al.</i> 2014)
<i>Taverniera cuneifolia</i> (Roth) Arn.	root culture	saponin	glycyrrhizic acid	<i>Penicillium fellutanum</i>	hyphae	hyphae	2 fold	(Awad <i>et al.</i> 2014)
<i>Taverniera cuneifolia</i> (Roth) Arn.	root culture	saponin	glycyrrhizic acid	<i>Fusarium moniliforme</i> Sheldon	hyphae	hyphae	2.5 fold	(Awad <i>et al.</i> 2014)
<i>Taverniera cuneifolia</i> (Roth) Arn.	root culture	saponin	glycyrrhizic acid	<i>Mucor hiemalis</i> Wehmer	hyphae	hyphae	3 fold	(Awad <i>et al.</i> 2014)

Table2. The accumulation of secondary metabolites induced by fungal elicitors and their related signaling molecules

Plants	cultured system	secondary metabolites	Types of secondary metabolites	Fungal	Fungal elicitors	Types of fungal elicitors	Related signaling molecules	Reference
<i>Artemisia annua</i>	cell culture	artemisinin	sesquiterpene lactone	<i>Fusarium oxysporum</i>	mycelium	mycelium	NO/H ₂ O ₂	(Zheng <i>et al.</i> 2010)s

						extract		
<i>Atractylodes lancea</i>	cell culture	volatile oil	mixture	<i>Cunninghamella la sp</i> AL4	crude extract	fungus extract	NO/H ₂ O ₂	(Fang <i>et al.</i> 2009)
<i>Atractylodes lancea</i>	whole plant	volatile oil	mixture	<i>Gilmaniella sp.</i>	fungus extract	fungus extract	NO mediates the process through SA and H ₂ O ₂ dependent pathways	(Wang <i>et al.</i> 2011)
<i>Catharanthus roseus</i>	cell culture	terpenoid	indole alkaloid	<i>Aspergillus niger</i>	fungus extract	fungus extract	Ca ²⁺ /ROS	(Zhao <i>et al.</i> 2001)
<i>Catharanthus roseus</i>	cell culture	terpenoid	indole alkaloid	yeast	yeast extract	fungus extract	JA	(Menke FL1 1999)
<i>Catharanthus roseus</i>	cell culture	catharanthine	indole alkaloid	<i>Penicillium citrinum</i>	cell wall	cell wall	NO(generated by NOS or NOS-like enzymes)	(Xu <i>et al.</i> 2005)
<i>Catharanthus roseus</i>	cell culture	catharanthine	indole alkaloid	<i>Aspergillus niger</i>	mycelia	mycelia extract	O ²⁻ rather than H ₂ O ₂	(Xu <i>et al.</i> 2005)
<i>Catharanthus roseus</i>	cell culture	catharanthine	indole alkaloid	<i>Aspergillus niger</i>	mycelia	mycelia extract	NO	(Xu <i>et al.</i> 2005)
<i>Camptotheca acuminata</i>	cell culture	camptothecin	indole alkaloid	<i>Phytophthora boehmeriae</i>	protein elicitor PB90	fungus extract	NO(NR-mediated NO generation)	(Lu <i>et al.</i> 2011)
<i>Cupressus lusitanica</i>	Callus culture	β-thujaplicin	tropolone	/	fungus extract	fungus extract	JA	(Zhao <i>et al.</i> 2001)
<i>Cupressus lusitanica</i>	cell culture	β-thujaplicin	tropolone	yeast	oligosaccharide fraction	fungus extract	Ca ²⁺ influx/G-proteins	(Zhao <i>et al.</i> 2003)
<i>Cupressus lusitanica</i>	cell culture	β-thujaplicin	tropolone	yeast	yeast extracts	fungus extract	cAMP/Ca ²⁺ / K ⁺ fluxes	(Zhao <i>et al.</i> 2004)a

<i>Cupressus lusitanica</i>	cell culture	β -thujaplicin	tropolone	yeast	yeast extracts	fungal extract	H ₂ O ₂ /NO	(Zhao <i>et al.</i> 2007)
<i>Cupressus lusitanica</i>	cell culture	β -thujaplicin	tropolone	yeast	yeast extracts	fungal extract	inositol 1,4,5-trisphosphate pathway via a Ca ²⁺ signaling pathway	(Zhao <i>et al.</i> 2004)b
<i>Cupressus lusitanica</i>	cell culture	β -thujaplicin	tropolone	yeast	yeast extracts	fungal extract	Ca ²⁺ /ETH/JA	(Zhao <i>et al.</i> 2004)
<i>Euphorbia pekinensis</i>	cell culture	isoeuphpekinen sin	terpenoid	<i>Fusarium sp.</i>	fungal elicitor	fungal elicitor	NO/SA	(Gao <i>et al.</i> 2012)
<i>Ginkgo biloba</i>	cell culture	flavonoid	flavonoid	<i>Sphaeropsis sp</i> B301	fungal elicitor	fungal elicitor	ABA	(Hao <i>et al.</i> 2010)
<i>Ginkgo biloba</i>	cell culture	flavonol glycoside	flavonol glycoside	<i>Phytophthora boehmeriae</i> PB90	protein(90 kD)	fungal extract	JA/SA	(Xu <i>et al.</i> 2009)
<i>Hypericum perforatum</i>	cell culture	hypericin	anthrone	<i>Phytophthora boehmeriae</i> PB90	protein(90 kD)	fungal extract	NADPH oxidase-mediated H ₂ O ₂ signaling pathway	(Qin <i>et al.</i> 2004)
<i>Hypericum perforatum</i>	cell culture	hypericin	anthrone	<i>Phytophthora cinnamoni</i>	cell wall extract	cell wall	JA	(Walker <i>et al.</i> 2002)
<i>Hypericum perforatum</i>	cell culture	hypericin	anthrone	<i>Aspergillum niger</i>	fungal extract	fungal extract	NO mediates it partially via a JA-dependent signaling pathway	(Xu 2005)
<i>Inonotus obliquus</i>	cell culture	antioxidant polyphenols	polyphenols	<i>Alternaria alternata</i>	fungal extract	fungal extract	NO mediates the process via a signalling pathway	(Zheng <i>et al.</i> 2009)

<i>Panax ginseng</i> C. A. Meyer	cell culture	saponin	saponin	<i>Colletotrichum lagenarium</i>	Cle	cell wall	independent of oxylipins or JA singlet oxygen /ethylene(ETH)	(Xu <i>et al.</i> 2005)
<i>Panax ginseng</i> C. A. Meyer	adventitious root	saponin	saponin	yeast	yeast extract	fungal extract	JA/H ₂ O ₂	(Rahimi <i>et al.</i> 2014)
<i>Petroselinum crispum</i>	cell culture	phytoalexin	mixture	<i>Phytophthora sojae</i>	crude cell wall	cell wall	Ca ²⁺ /O ₂ ⁻	(Jabs <i>et al.</i> 1997)
<i>Pueraria thomsonii</i> Benth.		puerarin	flavonoid	<i>Penicillium citrinum</i>	fungal extract	fungal extract	NO might mediate it through SA- and JA-dependent signal pathways	(Xu <i>et al.</i> 2006)
<i>Sanguinaria canadensis</i> L.	cell culture	benzophenanthridine alkaloid	alkaloid	<i>Penicillium expansum</i>	fungal extract	fungal extract	G proteins	(Mahady <i>et al.</i> 1998)
<i>Solenostemon scutellarioides</i>	whole plant	rosmarinic acid		<i>Aternaria alternata</i> / <i>Aspergillus niger</i> / <i>Fusarium solani</i>	fungal extract	fungal extract	JA/H ₂ O ₂	(Dewanjee <i>et al.</i> 2014)
<i>Sorbus aucuparia</i>	cell culture	aucuparin	biphenyl	yeast	yeast extract	yeast extract	H ₂ O ₂ rather than that of O ₂ ⁻	(Qiu <i>et al.</i> 2012)
<i>Taxus yunnanensis</i>	cell culture	taxol	diterpene	<i>Fusarium sp.</i>	cerebroside	fungal extract	NO	(Wang <i>et al.</i> 2004)
<i>Taxus chinensis</i>	cell culture	taxol	diterpene	/	mycelial wall	mycelial wall	SA	(Yu <i>et al.</i> 2001)

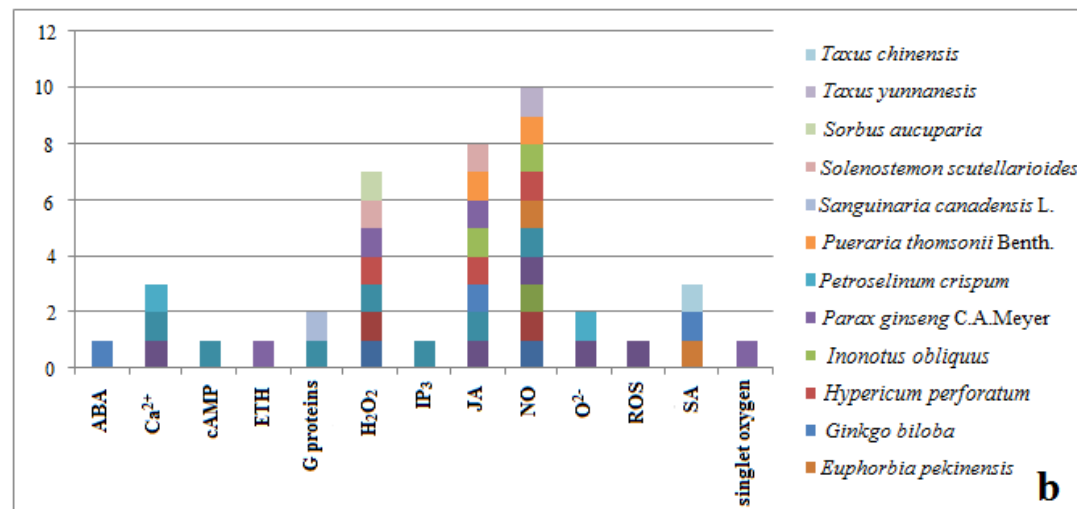
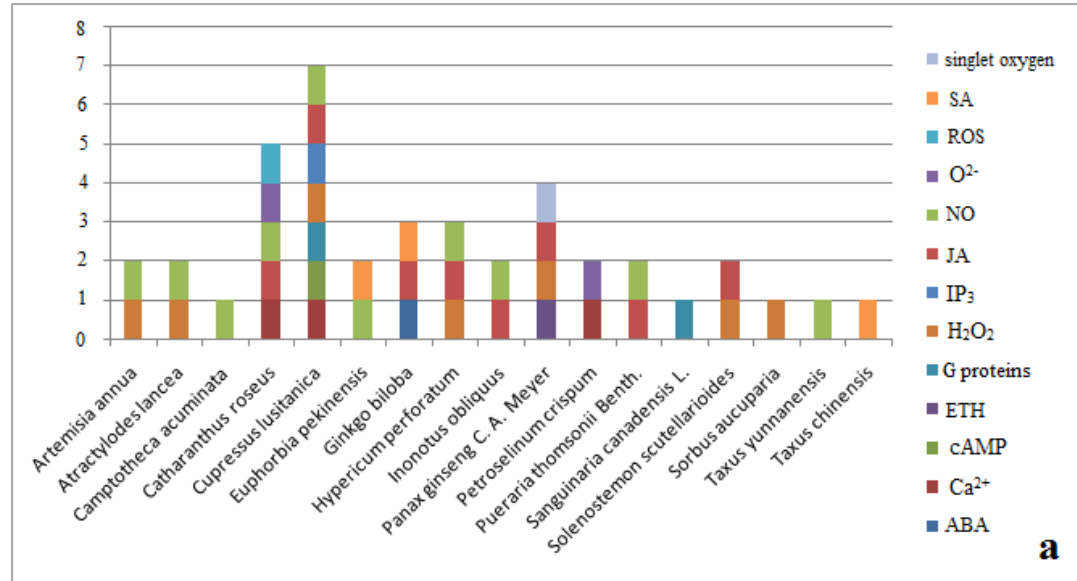


Figure 1. a. The signal molecules which have been investigated in medicinal plants induced by fungal elicitors. b. The frequency of each signaling molecule having been studied in the process of secondary metabolites accumulation induced by fungal elicitors in medicinal plants.

Figure 1.a. summarizes the signal molecules which are involved in different kinds of medicinal plants in fungal elicitor-inducing process. The figure displays several signaling molecules been studied in *Artemisia annua*, *Atractylodes lancea*, *Camptotheca acuminata*, *Catharanthus roseus*, *Cupressus lusitanica*, *Euphorbia pekinensis*, *Ginkgo biloba*, *Hypericum perforatum*, *Inonotus obliquus*, *Panax ginseng* C. A. Meyer, *Petroselinum crispum*, *Pueraria thomsonii* Benth., *Sanguinaria canadensis* L., *Solenostemon scutellarioides*, *Sorbus aucuparia*, *Taxus yunnanensis* and *Taxus chinensis*. We can see that the fungal elicitor-inducing secondary metabolites accumulation in *Cupressus lusitanica* are studied most frequently, involving Ca^{2+} , cAMP, G protein, H_2O_2 , IP_3 , JA, NO. That is to say that *Cupressus lusitanica* are the most commonly researched medicinal plant about signal transduction so far. The next in rank is *Catharanthus roseus* and *Panax ginseng*. We can study the signal transduction of secondary metabolites accumulation in other medicinal plants induced by fungal elicitor according to the mature approach applied in the research of *Cupressus lusitanica*, *Catharanthus roseus* and *Panax ginseng*. With the further study in other medicinal plants, we can try to find the similarities and differences in different medicinal plants and summarize the rule of signal transduction of secondary metabolites accumulation induced by fungal elicitor in medicinal plants. b. shows the frequency of the signal molecule having been studied in fungal-inducing process in medicinal plants so far. We can see that NO, ABA, Ca^{2+} , cAMP, ETH, G protein, IP_3 , O_2^- , ROS, H_2O_2 and JA are related to the secondary metabolism induced by fungal elicitors in medicinal plants. Among these signaling molecules, NO is the signaling molecule which is studied most frequently and followed by H_2O_2 and JA. This illustrates that these three signaling molecules may be relevant widely to the signal transduction of secondary metabolism induced by fungal elicitors in medicinal plants. That is to say NO, JA, H_2O_2 may be the essential signaling molecules in the process of fungal-induced secondary metabolism though more research is needed to support this argument. On the other hand, ABA, Ca^{2+} , cAMP, ETH, G protein, IP_3 , O_2^- , ROS and singlet oxygen are less studied in fungal-induced secondary metabolism. Therefore, we can pay more attention to the study of these signal molecules for improving the whole lines of signal transduction.

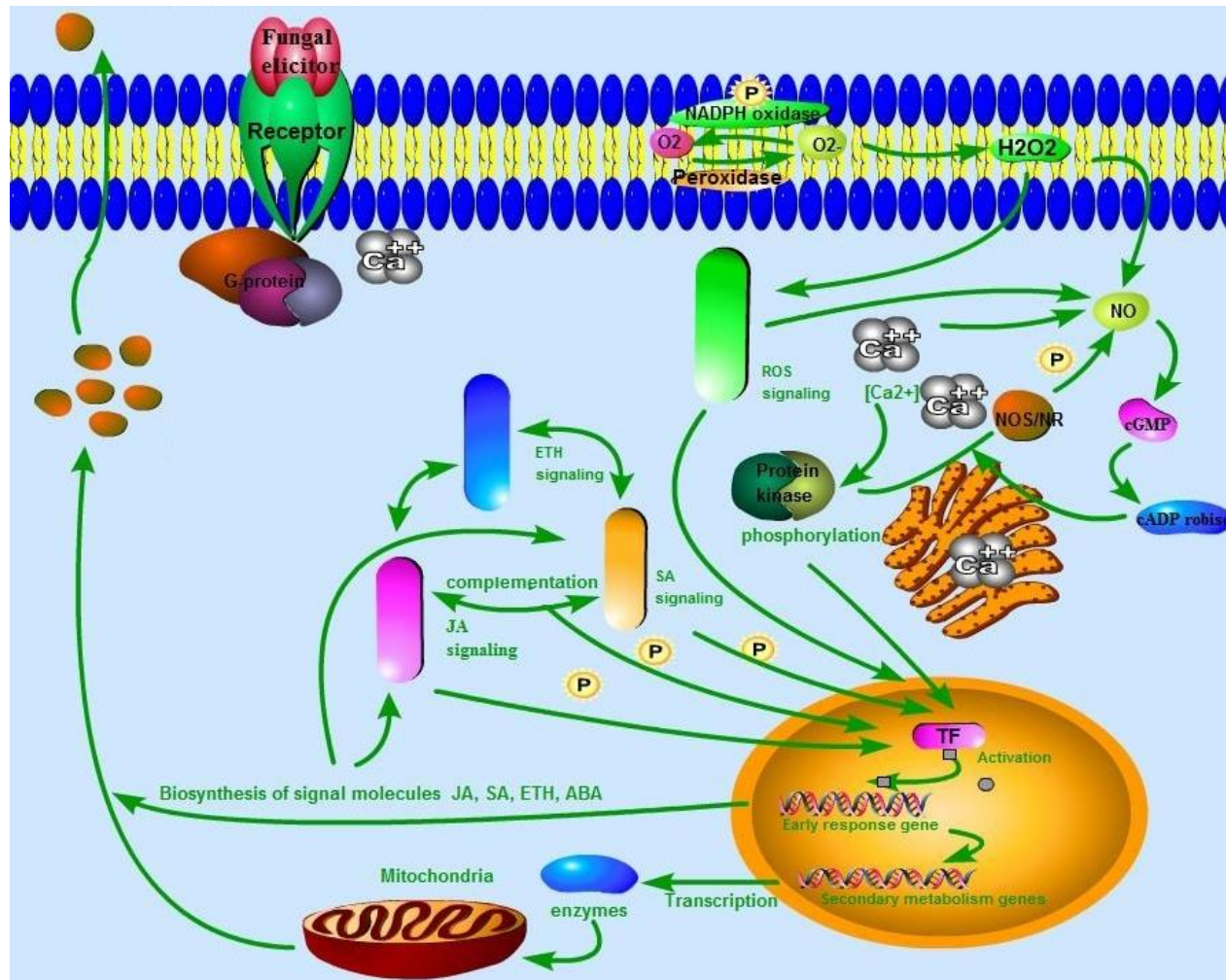
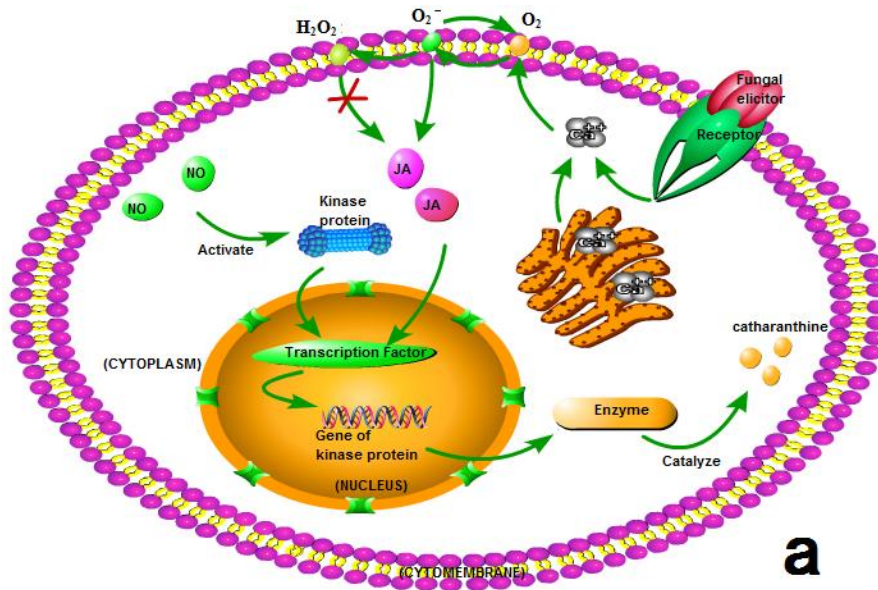


Figure2. The signaling pathway of fungal elicitor inducing secondary metabolites synthesis in plant cell

Fungal elicitors are identified and combined by receptors selectively on cell membrane, next the expression of related genes is regulated in the nucleus through complicated signal transduction pathways, and ultimately this activates the defensive secondary metabolism system to accumulate specific secondary metabolites. There are many signal molecules involved in the fungal elicitors-induced secondary metabolites in medical plants, such as Ca^{2+} ,

cAMP, inositol phosphate, G protein, salicylic acid, jasmonic acid, NO, ETH and so on. The signal transduction is intricacy and several signal molecules interact and talk with one another under different circumstances. In general, fungal elicitors cause the ion channels to open and G protein coupling through IP_3 as intracellular second messengers. The production of ROS through oxidative burst is common and universal. O_2^- and H_2O_2 are transformed mutually and mediate different signal pathway in various medical plants and NO can respectively delivery the signaling through dependent- or independent- oxidative burst signaling pathway. NO can promote the accumulation of SA which can hold up the synthesis of JA in plant cells There is a relationship of mutual inhibition but also special coordination complementary between SA and JA signaling pathways. All those signal molecules are involved in the accumulation of secondary metabolites in fungal-induced medical plants however, the mechanism is clearly defined, but they eventually gather into the response of transduction factors which is a bridge between signal molecules and gene expression.



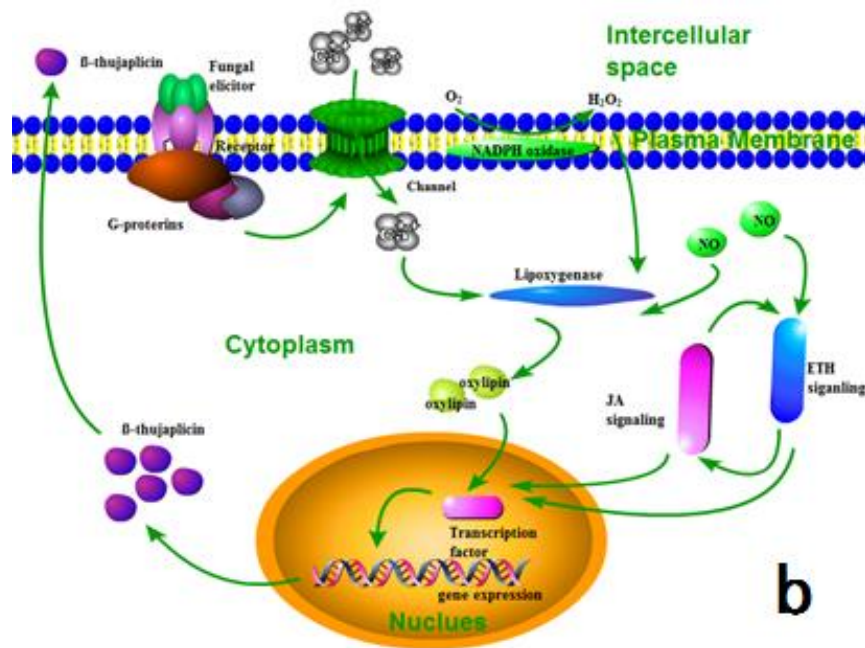
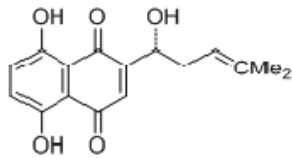


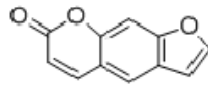
Figure 3 a. Fungal elicitor signaling pathway leading to catharanthine biosynthesis in *Catharanthus roseus* cell cultures. b. Fungal elicitor signaling pathway leading to β -thujaplicin biosynthesis in the cell of *Cupressus lusitanica*.

a. Ca^{2+} influx is a prerequisite for an elicitor-triggered oxidative burst as the first message transducer. Due to the oxidative burst, a substantial lipid peroxidation is related to indole alkaloid production. Thus fungal elicitor-induced indole alkaloid accumulation in *Catharanthus roseus* cell cultures is mediated at least partially by ROS or lipid peroxidation via the jasmonate signaling pathway. O_2^- rather than H_2O_2 from oxidative burst was demonstrated to be necessary for mediating fungal elicitor-induced catharanthine biosynthesis. NO released from SNP triggers fungal elicitor-induced terpenoid indole alkaloid biosynthesis of *C. roseus* cells through a protein kinase-dependent signal pathway. b. Fungal elicitor signaling pathway leading to β -thujaplicin biosynthesis in *Cupressus lusitanica* cell cultures. The ethylene and jasmonate signaling pathways can be regulated upstream by Ca^{2+} whose influx negatively regulates ethylene production, and differentially regulates fungal elicitor- or methyl jasmonate-stimulated ethylene production and G-proteins may mediate elicitor signals to the jasmonate pathway. The ethylene and jasmonate pathways interact in mediating β -thujaplicin production, with the jasmonate pathway controlling the production and the ethylene pathway acting as a fine modulator for accumulation of β -thujaplicin (Zhao *et al.* 2004). Reactive oxygen species (ROS) and nitric oxide (NO) signaling interact in cell death induction and β -thujaplicin production in *Cupressus lusitanica* cell cultures. Yeast elicitor

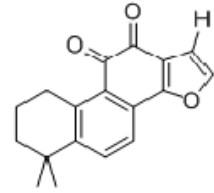
activates multiple signal components such as GTP-binding proteins, Ca^{2+} influx, and protein kinases. Following O_2^- , H_2O_2 and NO generation in elicited *C. lusitanica* cell cultures, jasmonate and ethylene accumulate to induce β -thujaplicin production. NO at low concentration induces cell death while high NO concentrations may inhibit ascorbate peroxidase (APX) activity and lipid peroxidation, probably through peroxynitrite. H_2O_2 and NO enhance each other's production and H_2O_2 is a positive inducer for β -thujaplicin production, most probably through hydroxyl radical-dependent lipid peroxidation-derived oxylipin signaling(Zhao *et al.* 2007).



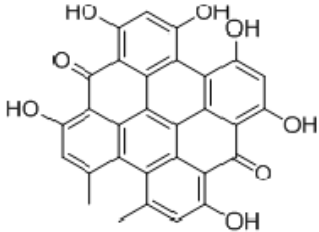
Shikonin, the only secondary metabolite that is successfully produced by large-scale plant cell culture



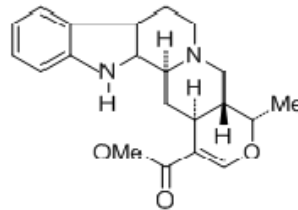
Psoralen, furocoumarine from *Psoralea corylifolia* L. cell induced by fungal elicitor



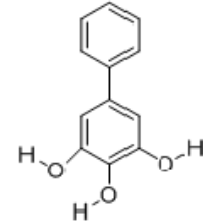
Tanshinone IIA, a diterpene which make big breakthrough in fungal elicitor-inducing process



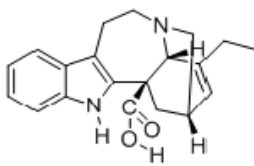
Hypericin, the secondary metabolite produced by *Hypericum perforatum* cell



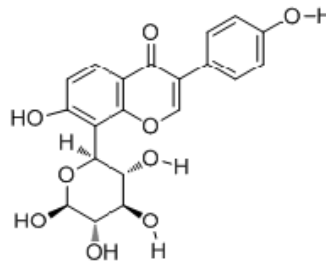
Ajmalicine, an extensively studied teepenoid indole from *Catharanthus roseus* cell



Aucuparin, the biphenyl compounds produced in *Sorbus aucuparia* cell



Catharanthine, a widely researched indole alkaloid from *Catharanthus roseus*



Puerarin, the flavonoid produced by *Pueraria thomsonii* Benth., which are used to study the signal transduction of secondary metabolism

Figure 4. Several secondary metabolites tightly related to fungal elicitor-inducing effects.