Research Progress on Biosynthesis and Regulation of Monoterpenoid Compounds

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Table S1： Whole-cell microbial production of representative monoterpenoids

MTP	Heterologous host	Key Engineering Strategy	Output (g/L)	Reference
Limonene	*Saccharomyces cerevisiae*	OLB pathway construction; Glucose-sensing promoter downregulating ERG20; MVA pathway enhancement; Limonene synthase engineering	0.9177	[1]
Limonene	*S. cerevisiae*	Downregulating ERG20; Enzyme optimization; Mitochondrial engineering; Fermentation process optimization; Enhancement of precursor and cofactor supply	2.63	[2]
Limonene	*Escherichia coli*	Enzyme engineering; MVA pathway; Fermentation process optimization	4.9	[3]
Menthol	*S. cerevisiae*	MVA pathway enhancement; Dynamic regulation of competitive pathways; Downstream pathway balance optimization	0.0063	[4]

MTP	Heterologous host	Key Engineering Strategy	Output (g/L)	Reference
Menthol	*E. coli*	MEP pathway optimization; Enzyme engineering	/	[5]
Menthol	*E. coli*	Enzyme discovery & engineering; MEP pathway; One-Pot Biocatalysis	1.5	[6]
α-Terpineol	*Penicillium digitatum*	Response Surface Methodology (RSM)	0.8339	[7]
α-Terpineol	*Sphingobium* sp.	Biotransformation condition optimization	240	[8]
α-Terpineol	*S. cerevisiae*	Enzyme Engineering; MVA pathway; Competitive pathway rewiring	0.0219	[9]
Carvone	*E. coli*	Balanced expression of P450/CDH16; Heterologous expression of plant-derived CYP71D18-ATR2-CD pathway	0.044	[10]
Perillaldehyde (PAE)	*E. coli*	MVA pathway; Enzyme engineering; Fed-Batch fermentation	0.415	[11]
Geraniol	*E. coli*	Fusion Tag engineering; MVA pathway	4.8	[12]
Geraniol	*S. cerevisiae*	Enzyme engineering; MVA pathway; Precursor (GPP) synthesis regulation	1.4	[13]
Geraniol	*Candida glycerinogenes*	Dynamic Regulation of Competitive Pathway; Expansion of Substrate Utilization; Bioprocess Optimization	5.2	[14]
Nerol	*E. coli*	Novel precursor pathway; MVA pathway	0.415	[15]
Nerol	*E. coli*	Novel Precursor Pathway; Site-Directed mutagenesis; Dephosphorylation enhancement	0.76	[16]
Linalool	*E. coli*	Bioinformatics-aided Enzyme Discovery	/	[17]
Linalool	*E. coli*	MEP pathway; Fermentation process optimization	1.52	[18]

MTP	Heterologous host	Key Engineering Strategy	Output (g/L)	Reference
Linalool	*S. cerevisiae*	MVA pathway; Enzyme engineering	5.87	[19]
Linalool	*S. cerevisiae*	IUP pathway; Enzyme engineering	5.2	[20]
Myrcene	*E. coli*	Enzyme Engineering; MVA pathway; Subcellular compartmentalization	0.0582	[21]
Myrcene	*S. cerevisiae*	Enzyme engineering; Host metabolic engineering; Advanced bioprocess design	0.0668	[22]
Myrcene	*S. cerevisiae*	Enzyme engineering; MVA pathway; Subcellular Compartmentalization	0.1426	[22]
Myrcene	*E. coli*	Enzyme engineering; High-Yield Geraniol Platform	5.73	[23]
α/β-Pinene	*E. coli*	Enzyme engineering; MVA pathway	/	[24]
α/β-Pinene	*E. coli*	Genetic element optimization; Enzyme Engineering; Precursor Pathway Optimization; Oxidation Module	1.87	[25]
α/β-Pinene	*E. coli*	Enzyme engineering; MVA pathway	1.0351	[26]
α/β-Pinene	*Rhodobacter sphaeroides*	MEP pathway; Genetic expression optimization	0.0001488	[27]
α/β-Pinene	*Yarrowia lipolytica*	MVA Pathway; Low-Cost Feedstock Utilization	0.5056	[28]
Borneol	*S. cerevisiae*	Enzyme engineering & discovery; MVA pathway	/	[29]
Borneol	*S. cerevisiae*	MVA pathway; Enzyme discovery & characterization	/	[30]
Borneol	*S. cerevisiae*	Enzyme engineering	0.1486	[31]

MTP	Heterologous host	Key Engineering Strategy	Output (g/L)	Reference
Borneol	*S. cerevisiae*	MVA pathway; Phosphatase discovery and engineering; Balancing cellular dephosphorylation metabolism	/	[32]
Borneol	*S. cerevisiae*	Enzyme engineering; MVA pathway	0.0230	[33]
Borneol	*E. coli*	Orthogonal precursor pathway; Enzyme engineering; Precursor Dephosphorylation Enhancement	0.0872	[16]
Camphor	*S. cerevisiae*	Enzyme engineering; MVA pathway	0.0235	[33]
Sabinene	/	Enzyme discovery	/	[34]
Sabinene	*E. coli*	Adaptive laboratory evolution; Multi-Omics analysis; Reverse engineering for validation	/	[35]
Sabinene	*S. cerevisiae*	Subcellular compartmentalization; Enzyme engineering & fusion; MVA pathway	0.1549	[36]

Table S2 Cell-free synthesis of representative monoterpenoid

MTP	Reaction system	Key Engineering Strategy	Output (g/L)	Reference
Limonene	Cell-Free Protein Synthesis (CFPS)	In vitro pathway reconstitution	0.610	[37]
Myrcene	Hybrid cell-free reaction system	Multi-enzyme cascade module assembly	/	[38]
Sabinene	Cell-free system	Computational modeling for bottleneck identification; ATP regeneration and phosphate cycling; Cofactor recycling and redox balancing	15.9	[39]

Table S3 Microbial biotransformation routes for representative monoterpenoids

MTP	Microbial strain	Transformation Strategy	Output (g/L)	Reference
Thujone	*Absidia coerulea*	Fungal whole-cell biotransformation	/	[40]

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