Two-Phase Fermentation Systems for Microbial Production of Plant-Derived Terpenes

Table S1. Summary of the fermentation results for monoterpenes, categorized by various chassis cells, fermentation types, the second phase, and production outputs.

Monoterpenes	Chassis cells	Fermentation types	Second phases	Titers (mg/L)	References
geraniol	*E. coli*	bioreactor	none	78.8	[1]
		flask	isopropyl myristate	2102.5	[2]
		bioreactor	isopropyl myristate	13190	[3]
		bioreactor	isopropyl myristate	2000	[1]
		flask	n-decane	182.5	[4]
		flask	n-decane	1119	[5]
		flask	n-decane	300	[6]
	S. cerevisiae	flask	none	5	[7]
		flask	none	36.04	[8]
		bioreactor	n-dodecane	227	[9]
		bioreactor	n-dodecane	293	[10]
		bioreactor	n-dodecane	1690	[11]
		bioreactor	isopropyl myristate	1680	[12]
	C. glutamicum	flask	n-dodecane	15.2	[13]
limonene	*E. coli*	flask	n-dodecane	435	[14]
		flask	n-dodecane	605	[15]
		flask	n-dodecane	214	[16]
		flask	isopropyl myristate	1290	[17]
		flask	diisononyl phthalate	37.8	[18]
		bioreactor	diisononyl phthalate	2700	[19]
		bioreactor	diisononyl phthalate	3630	[20]
	S. cerevisiae	flask	none	62.31	[21]
		flask	n-dodecane	0.12	[22]
		flask	n-dodecane	1.48	[23]
		flask	n-dodecane	2580	[24]
		flask	n-dodecane	166	[25]
		flask	n-dodecane	76	[26]
		bioreactor	n-dodecane	2630	[27]
		flask	isopropyl myristate	917	[28]
		flask	isopropyl myristate	2230	[29]
	R. toruloides	tube	n-dodecane	393.5	[30]
		flask	n-dodecane	358.1	[31]
	A. gossypii	flask	n-dodecane	336.4	[32]

	Y. lipolytica	flask	n-dodecane	23.56	[33]
		bioreactor	n-dodecane	165.3	[34]
	Synechococcus sp.	flask	n-dodecane	4	[35]
		flask	n-dodecane	6.7	[36]
	cyanobacteria	flask	isopropyl myristate	16.4	[37]
perillyl alcohol	*E. coli*	flask	resin	105	[38]
		bioreactor	n-dodecane	87	[39]
linalool	*E. coli*	flask	none	63	[40]
		flask	n-nonane	1054	[41]
		flask	n-dodecane	505	[42]
		flask	isopropyl myristate	1250	[43]
		bioreactor	isopropyl myristate	1523.2	[44]
	S. cerevisiae	flask	none	0.095	[45]
		bioreactor	none	0.26	[46]
		bioreactor	none	23.45	[47]
		bioreactor	none	0.24	[46]
		flask	isopropyl myristate	53.14	[48]
		flask	isopropyl myristate	80.9	[49]
	Y. lipolytica	flask	n-dodecane	6.96	[50]
		flask	isopropyl myristate	109.6	[51]
	P. ananatis	tube	isopropyl myristate	5600	[52]
		bioreactor	isopropyl myristate	10900	[53]
cineole	*E. coli*	flask	n-dodecane	21	[54]
		flask	n-dodecane	653	[42]
		flask	n-nonane	116.8	[55]
	S. cerevisiae	bioreactor	none	1100	[56]
strictosidine	*S. cerevisiae*	flask	none	0.5	[57]
		bioreactor	none	50	[58]
sabinene	*E. coli*	flask	none	150	[59]
		bioreactor	none	2650	[60]
	S. cerevisiae	flask	n-dodecane	17.5	[61]
pinene	*E. coli*	bioreactor	none	970	[62]
		flask	n-dodecane	166.5	[63]
		flask	n-dodecane	140	[59]
		flask	n-dodecane	104.6	[64]
	S. cerevisiae	flask	isopropyl myristate	11.7	[65]
	C. glycerinogenes	flask	n-dodecane	6	[66]
myrcene	*E. coli*	flask	n-dodecane	58.19	[67]
		flask	isopropyl myristate	1250	[43]

Abbreviation of microorganisms*: E. coli: Escherichia coli; S. cerevisiae: Saccharomyces cerevisiae*; *C. glutamicum:*

Corynebacterium glutamicum; R. toruloides: Rhodotorula toruloides; A. gossypii: Ashbya gossypii; Y. lipolytica: Yarrowia lipolytica; P. ananatis: Pantoea ananatis; C. glycerinogenes: Candida glycerinogenes

Table S2. Summary of the fermentation results for sesquiterpenes, categorized by various chassis cells, fermentation types, the second phase, and production outputs.

Sesquiterpenes	Chassis cells	Fermentation types	Second phases	Titers (mg/L)	References
amorphadiene	*E. coli*	flask	none	112.2	[68]
		tube	n-dodecane	180	[69]
		flask	n-dodecane	201	[70]
		flask	n-dodecane	290	[71]
		flask	n-dodecane	293	[72]
		tube	n-dodecane	300	[73]
		flask	n-dodecane	331.7	[74]
		flask	n-dodecane	404.8	[75]
		flask	n-dodecane	500	[76]
		flask	n-dodecane	700	[77]
		flask	n-dodecane	1400	[78]
		bioreactor	n-dodecane	500	[79]
		bioreactor	n-dodecane	3550	[80]
		bioreactor	n-dodecane	29700	[81]
		bioreactor	n-dodecane	30000	[82]
	S. cerevisiae	flask	n-dodecane	0.6	[83]
		flask	n-dodecane	54.6	[84]
		flask	n-dodecane	64	[73]
		flask	n-dodecane	120	[85]
		flask	n-dodecane	153	[86]
		flask	n-dodecane	497	[87]
		bioreactor	n-dodecane	41000	[88]
		flask	isopropyl myristate	4000	[89]
		bioreactor	methyl oleate	40000	[89]
		bioreactor	methyl oleate	25000	[90]
	Y. lipolytica	flask	n-dodecane	171.5	[91]
	R. toruloides	bioreactor	n-dodecane	36	[92]
	B. subtilis	flask	n-dodecane	20	[93]
	S. elongatus	flask	n-hexan/n-decane	19.8	[94]
α-farnesene	*E. coli*	flask	n-decane	380	[95]
		flask	n-decane	1100	[96]
	S. cerevisiae	bioreactor	n-dodecane	23.37	[97]
		flask	n-dodecane	1477.2	[98]

		bioreactor	n-dodecane	930	[99]
		bioreactor	n-dodecane	170	[100]
		bioreactor	n-dodecane	10400	[98]
		bioreactor	poly alpha olefins	130000	[84]
	Y. lipolytica	flask	n-dodecane	1700	[101]
		bioreactor	n-dodecane	260	[102]
		bioreactor	n-dodecane	10200	[103]
		bioreactor	n-dodecane	2570	[104]
		bioreactor	n-dodecane	25550	[101]
	S. elongatus	flask	n-dodecane	4.6	[105]
		Not mentioned	n-dodecane	1.2	[106]
	P. pastoris	flask	n-dodecane	2560	[107]
	Anabaena sp.	flask	resin	0.3054	[108]
β-farnesene	*E. coli*	flask	n-decane	5290	[109]
		bioreactor	n-decane	10310	[110]
		bioreactor	n-decane	8740	[111]
		bioreactor	n-decane	4060	[112]
	S. cerevisiae	bioreactor	poly alpha olefins	130000	[84]
	Y. lipolytica	glass tubes	n-dodecane	955	[113]
		bioreactor	n-decane	22800	[114]
bisabolene	*E. coli*	tube	n-dodecane	1100	[115]
		flask	n-dodecane	1150	[116]
		flask	n-dodecane	0.435	[117]
		bioreactor	n-dodecane	900	[118]
		bioreactor	canola oil	9100	[119]
	S. cerevisiae	flask	n-dodecane	900	[118]
		flask	n-dodecane	994	[118]
		bioreactor	n-dodecane	5200	[88]
	Synechococcus sp.	flask	n-dodecane	0.6	[35]
		bioreactor	n-dodecane	22.5	[120]
	C. reinhardtii	flask	n-dodecane	11	[121]
	R. toruloides	bioreactor	n-dodecane	680	[92]
nerolidol	*E. coli*	bioreactor	n-dodecane	16000	[122]
	S. cerevisiae	flask	n-dodecane	100	[123]
		flask	n-dodecane	497	[124]
		flask	n-dodecane	392	[125]
		bioreactor	n-dodecane	1711	[126]
		bioreactor	n-dodecane	5500	[125]
		bioreactor	n-dodecane	7010	[127]
α-humulene	*E. coli*	bioreactor	resin	60.2	[128]

		bioreactor	n-dodecane	958	[129]
	S. cerevisiae	bioreactor	n-dodecane	1726.78	[130]
patchoulol	*E. coli*	bioreactor	n-dodecane	970	[131]
		bioreactor	isooctane	40	[132]
	S. cerevisiae	flask	n-dodecane	42.1	[133]
		bioreactor	n-dodecane	467	[134]
		bioreactor	n-dodecane	1632	[135]
valencene	*S. cerevisiae*	flask	n-dodecane	31	[136]
		flask	n-dodecane	1.305	[137]
		bioreactor	n-dodecane	264.6	[138]
	Y. lipolytica	flask	n-dodecane	22.8	[139]
	C. glutamicum	flask	n-dodecane	2.41	[140]
	R. sphaeroides	flask	n-dodecane	352	[141]
	Synechocystis sp.	flask	isopropyl myristate	9.6	[142]
germacrene A	*E. coli*	flask	none	6.325	[143]
		flask	n-dodecane	126.4	[144]
		flask	n-dodecane	364.26	[145]
		bioreactor	n-dodecane	3520	[146]
	S. cerevisiae	flask	n-dodecane	375	[147]
		flask	n-dodecane	190	[148]
		flask	n-dodecane	469	[149]
		flask	n-dodecane	309.8	[150]
	P. pastoris	bioreactor	n-dodecane	1900	[151]
	O. polymorpha	bioreactor	n-dodecane	4700	[152]
	Y. lipolytica	bioreactor	isopropyl myristate	39000	[153]
α-santalene	*E. coli*	bioreactor	isopropyl myristate	2916	[154]
	S. cerevisiae	flask	n-dodecane	92	[155]
		bioreactor	n-dodecane	163	[156]
	Y. lipolytica	bioreactor	n-dodecane	27.92	[157]
β-caryophyllene	*E. coli*	flask	none	100	[158]
		bioreactor	none	1520	[159]
		bioreactor	none	1050	[160]
		bioreactor	n-dodecane	5142	[161]
	S. cerevisiae	bioreactor	n-dodecane	2949.1	[162]
α-cuprenene	*X. dendrorhous*	flask	n-dodecane	80	[163]
viridiflorol	*E. coli*	bioreactor	n-dodecane	25700	[82]
longifolene	*E. coli*	bioreactor	n-decane	382	[164]
(+)-zizaene	*E. coli*	bioreactor	resin	211	[165]
valerenadiene	*E. coli*	flask	n-decane	62	[166]
protoilludene	*E. coli*	flask	n-decane	1199	[167]
farnesol	*E. coli*	flask	methyl oleate	1419	[168]

	S. cerevisiae	flask	none	70	[169]
epi-isozizaene	*E. coli*	bioreactor	n-decane	727.9	[170]
α-isocomene	*E. coli*	bioreactor	n-decane	77.5	[170]
pentalenene	*E. coli*	bioreactor	n-decane	780.3	[170]
α-neoclovene	*S. cerevisiae*	bioreactor	n-dodecane	487.1	[162]
valerenic acid	*S. cerevisiae*	flask	n-dodecane	4	[171]
zerumbone	*S. cerevisiae*	bioreactor	n-dodecane	40	[172]
prespatane	*R. toruloides*	bioreactor	n-dodecane	1173.6	[173]
santalols	*S. cerevisiae*	bioreactor	n-dodecane	1300	[174]
α-santalol	*S. cerevisiae*	bioreactor	n-dodecane	1200	[174]
zerumbone	*S. cerevisiae*	bioreactor	n-dodecane	40	[172]

Abbreviation of microorganisms*: B. subtilis: Bacillus subtilis; S. elongatus: Synechococcus elongatus; P. pastoris: Pichia pastoris; C. reinhardtii: Chlamydomonas reinhardtii; R. sphaeroides: Rhodobacter sphaeroides; O. polymorpha: Ogataea polymorpha; X. dendrorhous: Xanthophyllomyces dendrorhous*

Table S3. Summary of the fermentation results for diterpenes, categorized by various chassis cells, fermentation types, the second phase, and production outputs.

Diterpenes	Chassis cells	Fermentation types	Second phases	Titers (mg/L)	References
miltiradiene	*S. cerevisiae*	bioreactor	none	488	[175]
		flask	n-dodecane	550	[176]
		bioreactor	n-dodecane	365	[177]
		bioreactor	n-dodecane	3500	[176]
gibberellic acid 3	*Y. lipolytica*	24-roundwell plates	none	12.8	[178]
gibberellic acid 4	*Y. lipolytica*	24-roundwell plates	none	17.3	[178]
taxadiene	*E. coli*	flask	none	1.3	[179]
		flask	n-dodecane	570	[180]
		bioreactor	n-dodecane	1000	[181]
		bioreactor	n-dodecane	1020	[181]
	S. cerevisiae	bioreactor	none	33	[182]
		flask	silica gel	8	[183]
		bioreactor	n-dodecane	129	[184]
		bioreactor	n-dodecane	127	[184]
	A. fumigatus	flask	immobilization	0.694	[185]
	A. tenuissima	flask	immobilization	0.388	[185]
oxygenated taxane	*S. cerevisiae*	bioreactor	n-dodecane	78	[186]
ent -kaurene	*E. coli*	bioreactor	none	578	[187]
		bioreactor	n-dodecane	624	[188]
	R. toruloides	bioreactor	n-dodecane	1400	[189]
geranylgeraniol	*S. cerevisiae*	bioreactor	none	3300	[190]
		flask	n-dodecane	374.02	[191]
		flask	n-dodecane	772.98	[191]
		bioreactor	n-dodecane	1310	[192]

		bioreactor	n-dodecane	5070	[191]
steviol	*E. coli*	bioreactor	none	1100	[193]
		bioreactor	n-dodecane	38.4	[188]
carnosic acid	*S. cerevisiae*	flask	none	25	[194]
		bioreactor	none	75.2	[194]
sclareol	*E. coli*	bioreactor	n-dodecane	1500	[195]
	S. cerevisiae	flask	n-dodecane	750	[196]
		flask	n-dodecane	403	[197]
		bioreactor	n-hexane	11400	[198]
levopimaradiene	*E. coli*	bioreactor	n-dodecane	700	[199]
levopimaric acid	*S. cerevisiae*	bioreactor	n-dodecane	400.3	[200]
rubusoside	*S. cerevisiae*	bioreactor	none	1400	[201]
		bioreactor	none	1369	[201]
rebaudiosides	*S. cerevisiae*	bioreactor	none	132.7	[201]
retinoids	*E. coli*	tube	n-dodecane	33	[202]
retinol	*S. cerevisiae*	bioreactor	n-dodecane	2349	[203]
	Y. lipolytica	bioreactor	n-dodecane	4860	[204]
13*R*-manoyl oxide	*S. cerevisiae*	bioreactor	n-dodecane	3000	[205]
forskolin	*S. cerevisiae*	flask	n-hexane	40	[206]
cis-abienol	*E. coli*	bioreactor	isopropyl myristate	634	[207]

Abbreviation of microorganisms*: A. fumigatus: Aspergillus fumigatus; A. tenuissima: Alternaria tenuissima*

Table S4. Summary of the fermentation results for triterpenes, categorized by various chassis cells, fermentation types, the second phase, and production outputs.

Triterpenes	Chassis cells	Fermentation types	Second phases	Titers (mg/L)	References
squalene	*S. cerevisiae*	bioreactor	none	445.6	[208]
		bioreactor	none	9472	[209]
		bioreactor	n-dodecane	207.02	[98]
ambrein	*E. coli*	flask	none	2.6	[98]
	P. pastoris	bioreactor	none	100	[210]
betulin	*S. cerevisiae*	flask	none	59.5	[211]
gypsogenin	*S. cerevisiae*	bioreactor	none	146.84	[212]
lupeol	*S. cerevisiae*	flask	none	200.1	[213]
		flask	none	23.6	[211]
α-amyrin	*S. cerevisiae*	flask	none	213.7	[214]
		bioreactor	none	1100	[214]
		bioreactor	none	175.15	[215]
		flask	none	11.97	[216]
β-Amyrin	*S. cerevisiae*	bioreactor	none	138.8	[217]
		bioreactor	none	108	[218]
		tube	none	6	[219]
		bioreactor	none	108.1	[220]

		bioreactor	none	44.92	[215]
ursolic acid	*S. cerevisiae*	flask	none	101.4	[221]
		flask	none	41.4	[221]
		bioreactor	none	62.5	[221]
		bioreactor	none	123.27	[222]
betulinic acid	*S. cerevisiae*	flask	none	91.6	[221]
		flask	none	16.5	[221]
		bioreactor	none	182	[223]
		bioreactor	none	1000	[211]
		bioreactor	none	26.7	[221]
	Y. lipolytica	flask	isopropyl myristate	51.87	[224]
morolic acid	*S. cerevisiae*	flask	none	68.3	[221]
		flask	none	24.3	[221]
		bioreactor	none	34.1	[221]
		flask	none	20.7	[225]
oleanolic acid	*S. cerevisiae*	bioreactor	none	606.9	[226]
	S. cerevisiae	flask	none	186.1	[226]
	S. cerevisiae	flask	none	21.4	[227]
	S. cerevisiae	bioreactor	none	155.58	[222]
ganoderic acid	*S. cerevisiae*	flask	none	14.5	[228]
maslinic acid	*S. cerevisiae*	bioreactor	none	384	[229]
corosolic acid	*S. cerevisiae*	bioreactor	none	141	[229]
alphitolic acid	*S. cerevisiae*	bioreactor	none	23	[229]
quillaic acid	*S. cerevisiae*	bioreactor	none	314.01	[212]
polpunonic acid	*S. cerevisiae*	tube	none	1.4	[230]
glycyrrhetinic acid	*S. cerevisiae*	bioreactor	none	18.9	[220]
dammarenediol-II	*S. cerevisiae*	bioreactor	none	15000	[231]
		flask	none	211.52	[232]
		bioreactor	none	8088.8	[233]
		bioreactor	methyl oleate/n-dodecane	1548	[234]
	E. coli	flask	none	8.63	[235]
protopanaxadiol	*S. cerevisiae*	flask	none	17.2	[227]
		bioreactor	none	235	[231]
		bioreactor	methyl oleate/n-dodecane	1189	[234]
		bioreactor	none	9054.5	[233]
		bioreactor	none	1436.6	[236]
protopanaxatriol	*S. cerevisiae*	flask	none	15.9	[227]
ginsenoside Rh2	*S. cerevisiae*	bioreactor	none	300	[237]
		flask	none	16.9	[238]
		bioreactor	none	2250	[233]
ginsenoside Rg3	*S. cerevisiae*	bioreactor	none	1.3	[239]

		flask	none	51.8	[238]
ginsenoside RF1	*S. cerevisiae*	flask	none	42.1	[240]
ginsenoside Rh1	*S. cerevisiae*	flask	none	92.8	[240]

Table S5. Summary of the fermentation results for tetraterpene, categorized by various chassis cells, fermentation types, the second phase, and production outputs.

Tetraterpenes	Chassis cells	Fermentation types	Second phases	Titers (mg/L)	References
β-carotene	*E. coli*	flask	none	503	[241]
		flask	none	464	[242]
		bioreactor	none	2100	[243]
		bioreactor	none	663	[244]
		bioreactor	none	3200	[245]
		bioreactor	none	390	[246]
	S. cerevisiae	tube	none	477.9	[247]
lycopene	*E. coli*	tube	none	77.85	[248]
		flask	none	3520	[248]
		flask	none	1440	[249]
		bioreactor	none	128	[250]
		flask	none	358.9	[251]
		flask	none	224	[252]
		bioreactor	none	2700	[253]
	S. cerevisiae	flask	none	2300	[254]
		bioreactor	none	2370	[255]
		bioreactor	none	1610	[256]
	Y. lipolytica	bioreactor	none	4200	[257]
	Mucor circinelloides	flask	none	54000	[258]
	R. rubrum	flask	none	15	[259]
	R. sphaeroides	flask	none	66.05	[260]
	H. mediterranei	flask	none	429.41	[261]
	P. pastoris	bioreactor	none	73.9	[262]
		flask	none	714	[263]
astaxanthin	*E. coli*	bioreactor	none	880	[264]
		bioreactor	none	1820	[265]
crocetin	*S. cerevisiae*	bioreactor	none	6.278	[266]
zeaxanthin	*E. coli*	flask	none	43.46	[267]
		bioreactor	none	722.46	[268]
	S. cerevisiae	tube	none	1.5	[269]
	P. putida	flask	none	51.3	[270]

Abbreviation of microorganisms*: R. rubrum: Rhodospirillum rubrum; H. mediterranei: Haloferax mediterranei; P. putida:*

Pseudomonas putida

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