

Supplementary material 1.

Table 1. Phytochemical analysis of CXE, BCE, and CXBCH preparations.

Test	Samples and materials		
	CXE	BCE	CXBCH Preparation
Qualitative			
Alkaloids	++	+	++
Flavonoids	++	++	++
Phenolic	++	++	++
Saponins	+	+	+
Triterpenoids	+	++	+
Quantitative			
Polyphenol	142.23 ppm	42.51 ppm	38.87 ppm
Flavonoids	116.41 ppm	31.74 ppm	56.86 ppm
Thymoquinone	-	54.71 mg/g	46.45 mg/mL
Curcumin	62.28 mg/mL	-	68.86 mg/mL

Supplementary material 2

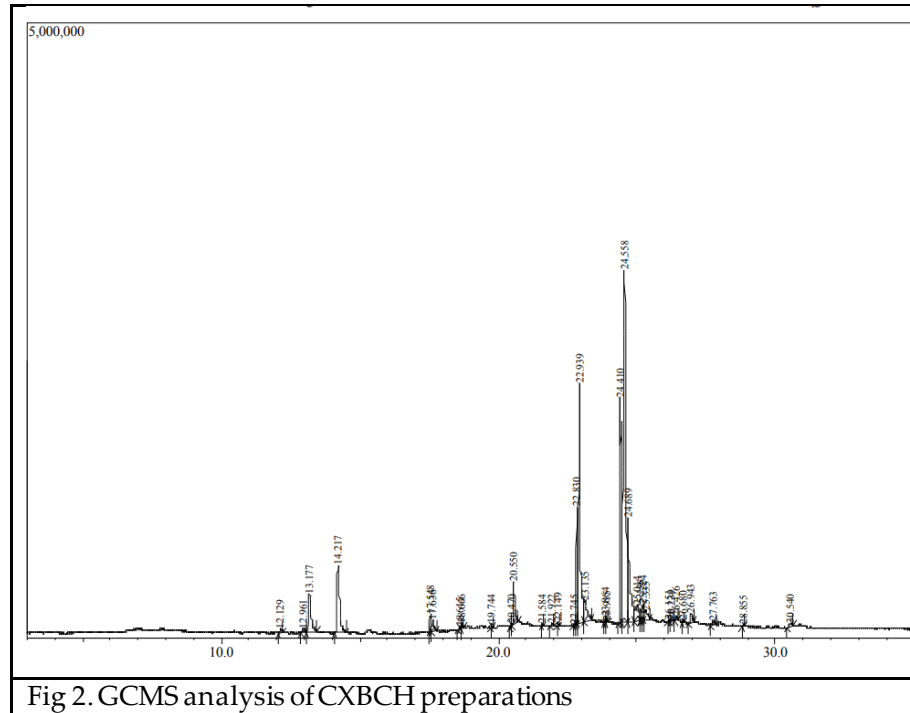
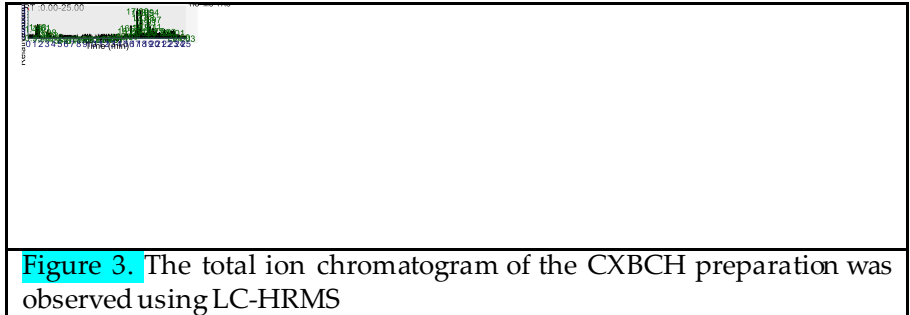


Table 2. profile volatile Compounds of CXBCH preparations, CXE, and BCE from the GCMS examination

No Peak	R.Time	I.Time	F.Time	Composition	Formula	Name
1	12.129	12.045	12.240	0.32	C15H24	1,6,10-dodecatriene, 7,11-dimethyl-3-methylene-, (e)-
2	12.961	12.870	13.080	0.32	C15H24	gamma.-curcumene
3	13.177	13.080	13.455	4.14	C15H22	benzene, 1-(1,5-dimethyl-4-hexenyl)-4-methyl-
4	14.217	14.090	14.495	6.82	C15H24	gamma.-curcumene
5	17.548	17.485	17.600	0.94	C15H22O	beta.-Elemenone (CAS)
6	17.636	17.600	17.765	0.76	C9H14N2O3S	n-(4-hydroxyphenyl)-n,n',n'-trimethylsulfamide
7	18.615	18.535	18.630	0.11	C15H22O2	6-(1-Hydroxymethylvinyl)-4,8a-dimethyl-3,5,6,7,8,8a-hexahydro-1H-naphthalen-2-one
8	18.666	18.630	18.750	0.27	C17H33Cl	7-Heptadecene, 1-chloro- (CAS)
9	19.744	19.710	19.780	0.12	C15H26O	Juniper camphor
10	20.470	20.415	20.505	0.10	C24H32O6	medrol acetate
11	20.550	20.505	20.705	3.04	C9H12O	Cc1cc(C)c(O)c(C)c1
12	21.584	21.550	21.640	0.08	C20H40O	3,7,11,15-Tetramethyl-2-hexadecen-1-ol
13	21.922	21.880	22.010	0.13	C12H22O	2-methyl-10-undecenal
14	22.149	22.110	22.205	0.12	C21H38O4	9-Octadecenoic acid, 12-(acetyloxy)-, methyl ester, [R-(Z)]- (CAS)
15	22.745	22.695	22.785	0.08	C12H22O2	cyclooctanecarbonic acid, 4-methyl-, ethylester
16	22.830	22.785	22.860	3.36	C18H36O2	Hexadecanoic acid, ethyl ester (CAS)
17	22.939	22.860	23.105	16.49	C16H32O2	Hexadecanoic acid (CAS)
18	23.135	23.105	23.365	2.06	C20H40O2	Eicosanoic acid (CAS)
19	23.864	23.795	23.895	0.24	C19H36O2	9-Octadecenoic acid, methyl ester (CAS)
20	23.915	23.895	23.975	0.10	C46H58N4O8	14'-epi-20'-deoxyvincovaline
21	24.410	24.345	24.465	10.99	C20H36O2	Ethyl linoleate
22	24.558	24.465	24.660	33.65	C16H30O2	9-Hexadecenoic acid (CAS)
23	24.689	24.660	24.925	8.88	C18H36O2	octadecanoic acid
24	25.014	24.925	25.110	2.08	C22H38O2	Cyclopropanecarboxylic acid, 2-[[2-[(2-ethylcyclopropyl)methyl]cyclopropyl]methyl]-, methyl ester (CAS)
25	25.136	25.110	25.170	0.56	C16H27NO4	6-Nitro-cyclohexadecane-1,3-dione
26	25.224	25.170	25.265	1.06	C18H36O3	Hexadecanoic acid, 2-hydroxyethyl ester (CAS)
27	25.335	25.265	25.485	1.12	C21H38O2	11,14-Eicosadienoic acid, methyl ester (CAS)
28	26.151	26.110	26.200	0.10	C18H32O2	9,12-Octadecadienoic acid (Z,Z)- (CAS)
29	26.239	26.200	26.360	0.18	C18H34O2	9-Octadecenoic acid (Z)- (CAS)
30	26.426	26.360	26.505	0.27	C20H40O2	Eicosanoic acid (CAS)
31	26.680	26.640	26.720	0.10	C20H37ClO2	2-Chloroethyl oleate
32	26.943	26.885	27.055	0.69	C21H40O3	Oleic acid, 3-hydroxypropyl ester (CAS)
33	27.763	27.680	27.875	0.35	C19H38O4	Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester (CAS)
34	28.855	28.780	28.895	0.09	C12H24O2	Decanoic acid, ethyl ester (CAS)
35	30.540	30.435	30.640	0.28	C20H38O3	9-Octadecenoic acid (Z)-, 2-hydroxyethyl ester (CAS)
Total				100.00		

Supplementary material 4



Supplementary material 5

Tabel 3. Formula, molecule name, RT, annotation delta mass and max area (absolute) observed with LC-HRMS from CXBCH preparations.

No	Name	Formula	Annot. DeltaMass [ppm]	Calc. MW	RT [min]	Area (Max.)
1	Linoleic acid	C18H32O2	-3.41	280.23927	22.713	73665569215
2	eremanthin	C15H18O2	-3.27	230.12993	17.869	49142859119
3	1,5-Anhydro-D-fructose	C6H10O5	-2.94	162.05235	1.57	23076928966
4	Oleic acid	C18H34O2	-3.18	282.25498	20.527	20748954114
5	1,5-Anhydro-6-deoxy-D-threo-hex-1-en-3-ulose	C6H8O4	-2.08	144.04196	1.606	16831135065
6	1-Linoleoyl glycerol	C21H38O4	-4.96	354.27525	21.601	16123655143
7	Monoolein	C21H40O4	-4.44	356.29108	23.058	15577251606
8	TURMERONE, AR-	C15H20O	-3.22	216.15072	17.516	10297107430
9	Meglutol	C6H10O5	-2.54	162.05241	3.029	10269644874
10	L- α -PALMITIN	C19H38O4	-4.13	330.27564	22.528	9837543783
11	9-Oxo-10(E),12(E)-octadecadienoic acid	C18H30O3	-3.01	294.21861	19.108	9468689328
12	(E)-6-hydroxyoctadec-4-enoic acid	C18H34O3	-3.02	298.2499	19.444	9449669222
13	Curcumin	C21H20O6	-3.55	368.12468	16.266	9142424073
14	(E,E)-alpha-Farnesene	C15H24	-3.33	204.18712	19.747	8176647345

15	S-Curcumene	C15 H22	-3.69	202.171 4	18.93 8	7151614 798
16	9(Z),11(E),13(E)-Octadecatrienoic Acid methyl ester	C19 H32 O2	-3.8	292.239 12	20.09 3	6795616 369
17	Pyrogallol	C6 H6 O3	-1.7	126.031 48	3.29	6146490 443
18	(2E)-3-(3-Hydroxyphenyl)acrylaldehyde	C9 H8 O2	-2.26	148.052 1	17.86 1	4610742 991
19	11(Z),14(Z)-Eicosadienoic acid	C20 H36 O2	-2.98	308.270 61	21.89 7	4532720 559
20	(-)-Camphor	C10 H16 O	-2.9	152.119 67	15.39 5	4482468 927
21	α -Eleostearic acid	C18 H30 O2	-2.41	278.223 91	19.15 1	4016574 114
22	NP-020521	C18 H32 O3	-2.87	296.234 29	19.14 8	3964161 053
23	Prednisone	C21 H26 O5	-4.41	358.176 45	16.46 4	3457086 374
24	(2S)-2,3-Dihydroxypropyl (11Z,14Z)-11,14-icosadienoate	C23 H42 O4	-3.37	382.307 02	19.25 2	3356497 775
25	2,2'-Methylenebis(4-methyl-6-tert-butylphenol)	C23 H32 O2	-3	340.239 21	21.28 2	2849183 680
26	Carvone	C10 H14 O	-2.35	150.104 11	18.92 1	2780665 813
27	3,4-Dihydrocadalene	C15 H20	-3.23	200.155 86	19.10 5	2407722 995
28	Oleamide	C18 H35 N O	-2.8	281.271 08	22.39 9	2172824 383
29	Monoolein	C21 H40 O4	-4.45	356.291 07	22.48 2	1982732 023
30	1-Stearoylglycerol	C21 H42 O4	-4.28	358.306 77	20.71 6	1962687 838
31	Etretinate	C23 H30 O3	-2.87	354.218 48	19.74 6	1948205 351

32	NP-019983	C20 H16 O6	-3.39	352.093 5	14.72 6	1934173 852
33	Phloroglucinol	C6 H6 O3	-1.55	126.031 5	3.555	1931287 884
34	Stearidonic acid	C18 H28 O2	-2.32	276.208 29	19.07 4	1815011 551
36	geranyl quinone	C16 H20 O2	-2.98	244.145 6	17.46 8	1656123 930
37	5,6,7-Trihydroxy-8-(3-methyl-2-buten-1-yl)-4-phenyl-2H-chromen-2-one	C20 H18 O5	-2.99	338.114 41	16.28 5	1552047 892
38	5-hydroxy-4-methoxy-5,6-dihydro-2H-pyran-2-one	C6 H8 O4	-2.47	144.041 9	3.556	1504039 499
39	Wighteone	C20 H18 O5	-2.6	338.114 54	16.63 6	1313576 685
40	(2S)-3-(4-Hydroxyphenyl)-2-([[(3S,4S,5R)-2,3,4-trihydroxy-5-(hydroxymethyl)tetrahydro-2-furanyl]methyl]amino)propanoic acid (non-preferred name)	C15 H21 N O8	-3.71	343.125 44	1.374	1253477 230
41	8Z,11Z,14Z-Eicosatrienoic acid	C20 H34 O2	-3.9	306.254 69	20.64 3	1239989 132
42	(+/-)12(13)-DiHOME	C18 H34 O4	-2.72	314.244 86	18.13 8	1175250 981
43	NP-011548	C18 H34 O3	-3.44	298.249 77	20.56 3	1122064 288
44	α -Linolenic acid	C18 H30 O2	-2.95	278.223 76	21.66 7	1080906 094
45	(-)-Caryophyllene oxide	C15 H24 O	-3.36	220.181 97	14.47 1	9963650 54.1
46	Curcumene	C15 H22	-3.69	202.171 4	17.40 1	9691705 27.2
47	α -Eleostearic acid	C18 H30 O2	-2.37	278.223 92	22.49 3	8732276 11.3
48	2,4-Dimethylbenzaldehyde	C9 H10 O	-2.78	134.072 79	19.35 5	7875235 27.3
49	(3 β ,24R,24'R)-fucosterolepoide	C29 H48 O2	-3.84	428.363 79	20.39 3	5945264 84.4

50	O-Demethylcurcumin	C20 H18 O6	-2.69	354.109 38	15.86 8	5810967 44.5
51	(16beta)-16,21-Epoxypregna-4,17-diene-3,11,21-trione	C21 H24 O4	-3.32	340.166 33	18.56 9	5386393 59.5
52	1-[(11Z,14Z)]-icosadienoyl-sn-glycero-3-phosphocholine	C28 H54 N O7 P	-3.18	547.362 05	18.92 4	5060813 86
53	(+/-)9-HpODE	C18 H32 O4	-3.04	312.229 11	18.05 6	4630656 94.7
54	16-Hydroxyhexadecanoic acid	C16 H32 O3	-2.33	272.234 51	21.83 2	4460572 99.6
55	(15Z)-9,12,13-Trihydroxy-15-octadecenoic acid	C18 H34 O5	-2.25	330.239 88	16.17 9	4326873 55.6
56	5-Methoxy-7-(4-hydroxy-3-methoxyphenyl)-1-phenyl-3-heptanone	C21 H26 O4	-3.17	342.182 02	19.46 4	4320299 34.4
57	3-Ethylphenol	C8 H10 O	-2.9	122.072 81	16.24	3855265 16.2
58	1,3,7-Trihydroxy-2,8-bis(3-methyl-2-buten-1-yl)-9H-xanthen-9-one	C23 H24 O5	4.96	380.164 26	22.71 1	3679616 42.2
59	1-Naphthol	C10 H8 O	-2.35	144.057 18	17.61 5	3609529 78.5
60	(±)9-HpODE	C18 H32 O4	-3.04	312.229 11	19.35 6	3395006 63.4
61	all-trans-4,4'-diapo-zeta-carotene	C30 H44	-2.68	404.343 22	18.90 1	3350970 27.5
62	1-Methyl-4-(1-methyl-2-propenyl)-benzene	C13 H18	-1.55	174.140 58	18.94 7	3255089 27.1
63	Vanillin	C8 H8 O3	-1.47	152.047 12	9.205	3144995 36.3
64	2-Ethyltoluene	C9 H12	-1.36	120.093 74	19.36 1	3029598 28.6
65	citaurin	C30 H40 O2	-3.05	432.301 51	22.04 6	2654243 39.3
66	13(S)-HOTrE	C18 H30 O3	-2.07	294.218 89	18.65 8	2533066 61.7

67	Tapentadol	C14 H23 N O	-2.48	221.177 42	11.72 7	2360887 94.5
68	(8Z,11Z,14Z)-heptadecatrienoic acid	C17 H28 O2	-2.16	264.208 36	20.12 4	2299076 37.4
69	3,6-Anhydro-1-O-palmitoylhexitol	C22 H42 O6	-2.8	402.297 01	23.00 7	2212833 35.7
70	Linoleoyl ethanolamide	C20 H37 N O2	-4.16	323.281 08	17.41 6	2131231 16.3
71	Ferulic acid	C10 H10 O4	-4.12	194.057 11	10.48 6	2067817 09.5
72	5-Pentylresorcinol	C11 H16 O2	-2.77	180.114 53	13.83 6	2025544 56.5
73	9(Z),11(E),13(E)-Octadecatrienoic Acid methyl ester	C19 H32 O2	-3.78	292.239 13	20.95 4	1983259 31.6
74	(11E)-15-Oxo-11-icosenoic acid	C20 H36 O3	-3.31	324.265 37	21.92 4	1923538 81.8
75	1-(7,8-Dimethoxy-2,2-dimethyl-2H-chromen-6-yl)ethanone	C15 H18 O4	-2.79	262.119 78	17.02 6	1902883 45.4
76	8-Hydroxy-5,8a-dimethyl-3-methylene-3a,4,4a,7,8,8a,9,9a-octahydronaphtho[2,3-b]furan-2(3H)-one	C15 H20 O3	-3.04	248.140 49	18.39	1892165 10
77	1-Stearoyl-2-hydroxy-sn-glycero-3-PE	C23 H48 N O7 P	2.24	481.317 92	21.91 4	1729003 35.8
78	12-oxo Phytodienoic Acid	C18 H28 O3	-2.51	292.203 11	16.93 5	1514229 30.9
79	(2R)-3-Hydroxy-2-[(9Z,12E)-9,12-octadecadienoyloxy]propyl 2-(trimethylammonio)ethyl phosphate	C26 H50 N O7 P	-2.74	519.331 06	21.04	1361617 00.3
80	DL-carvone	C10 H14 O	-2.35	150.104 11	13.72 3	1350441 05.6
81	9(S)-HpOTrE	C18 H30 O4	-1.9	310.213 82	16.95 4	1271327 71.3
82	(15Z)-9,12,13-Trihydroxy-15-octadecenoic acid	C18 H34 O5	-2.25	330.239 88	16.71 1	1231487 09.5

83	3-oxopalmitic acid	C16 H30 O3	-2.37	270.218 85	20.85 7	1148304 50.8
84	6-Hydroxy-2,3,4-trimethoxybenzoic acid	C10 H12 O6	-2.35	228.062 85	1.482	1142056 34.8
85	2(N)-Methyl-norsalsolinol	C10 H13 N O2	-2.13	179.094 25	9.838	8962733 3.47
86	4-methoxy-6-(prop-2-en-1-yl)-2H-1,3-benzodioxole	C11 H12 O3	-2.14	192.078 23	13.07 2	8738365 7.19
87	Nicotinic acid	C6 H5 N O2	-2.03	123.031 78	21.42 2	8200516 6.33
88	(9S,10S)-10-Hydroxy-9-(phosphonooxy)octadecanoic acid	C18 H37 O7 P	-3.27	396.226 39	20.03	7509159 6.97
89	NP-015687	C19 H16 O4	-2.73	308.104 02	16.56	7378551 6.74
90	Citral	C10 H16 O	-2.98	152.119 66	17.56 5	7078606 1.68
91	Methylstyrylpyron	C14 H12 O4	-2.6	244.072 92	16.71	7035768 5.76
92	2,3,4,9-Tetrahydro-1H- β -carboline-3-carboxylic acid	C12 H12 N2 O2	-1.91	216.089 46	7.296	6222263 3.61
93	(2S)-2,3-Dihydroxypropyl (9Z)-9-hexadecenoate	C19 H36 O4	-3.42	328.260 24	19.81 9	6179148 1.82
94	(+)-(S)-Carvone	C10 H14 O	-2.35	150.104 11	11.27 5	6153951 8.31
95	1-Methyl-1,2,3,4-tetrahydro- \hat{P} -carboline-3-carboxylic acid	C13 H14 N2 O2	-3.78	230.104 66	8.362	5275379 7.35
96	cis-12-Octadecenoic acid methyl ester	C19 H36 O2	-3.7	296.270 43	20.54 5	5150668 3.22
97	m-Cresol	C7 H8 O	0.05	108.057 52	17.86 9	5115550 4.38
98	(2E,4E,7E)-2,4,7-Decatrienoic acid	C10 H14 O2	-2.37	166.098 99	10.70 9	5107034 4.43
99	Ethyl oleate	C20 H38 O2	-4.8	310.285 69	22.24 1	5046085 1.23

100	Apocynin	C9 H10 O3	-2.23	166.062 62	12.91 4	4961521 4.04
101	(-)-isopiperitenone	C10 H14 O	-2.46	150.104 1	11.49 4	4818211 2.4
102	NP-003672	C15 H14 O2	-2.89	226.098 73	14.55 5	4674234 4.31
103	Ibuprofen	C13 H18 O2	-2.29	206.130 21	12.95 6	4537867 0.95
104	4-(4-hydroxy-2-methoxy-3,5,6-trimethylbenzoyloxy)-2-methoxy-3,5,6-trimethylbenzoic acid	C22 H26 O7	-2.93	402.166 67	13.06 3	4079398 2.98
105	Quercetin	C15 H10 O7	-2.64	302.041 85	13.54 7	3932029 9.41
106	3,4-Dihydroxycinnamaldehyde	C9 H8 O3	-2.2	164.046 98	14.03 5	3921583 0.21
107	N-[(2E)-3-(3,4-Dihydroxyphenyl)-2-propenoyl]tryptophan	C20 H18 N2 O5	-4.69	366.119 86	22.53 2	3872685 0.42
108	Palmitic acid	C16 H32 O2	-2.97	256.239 47	21.61 2	3835196 1.64
109	Corchoric fatty acid F	C18 H32 O5	-2.37	328.224 2	15.44 9	3675739 8.95
110	4-Ethylguaiaicol	C9 H12 O2	-2.23	152.083 39	14.91 1	3290740 8.94
111	trans-10-Heptadecenoic acid	C17 H32 O2	-2.66	268.239 52	17.86 1	3220574 0
112	3-dehydro-6-deoxoteasterone	C28 H48 O3	-4.18	432.358 54	21.73 1	3083786 4.78
113	geranyl quinone	C16 H20 O2	-2.98	244.145 6	22.51 8	3020629 3.08
114	NP-015559	C17 H14 O7	-3.03	330.072 95	15.18 6	2727792 1.65
115	(10S)-Juvenile hormone III acid diol	C15 H26 O4	-2.79	270.182 36	14.93 4	2472498 6.51
116	4-Coumaric acid	C9 H8 O3	-1.73	164.047 06	10.03 8	2469656 0.89

117	10,16-Dihydroxyhexadecanoic acid	C16 H32 O4	-2.45	288.229 35	17.97 5	2010315 8.23
118	COSMENE	C10 H14	-1.64	134.109 33	11.29	1881719 8.48
119	3-Dimethylallyl-4-hydroxymandelic acid	C13 H16 O4	-3.89	236.103 94	13.87 9	1847392 7.57
120	Levallorphan	C19 H25 N O	-1.7	283.193 13	11.49 9	1823620 9.55
121	12-HSA	C18 H36 O3	-3.19	300.265 49	17.29 2	1771318 7.6
122	(2Z)-2-(4-Hydroxybenzylidene)heptanoic acid	C14 H18 O3	-0.1	234.125 57	15.18 2	1731720 7.37
123	Vitamin A	C20 H30 O	-2.89	286.228 84	20.76 5	1696151 6.47
124	coenzyme Q2	C19 H26 O4	-3.9	318.181 87	18.49	1508009 0.56
125	Octyl gallate	C15 H22 O5	-2.64	282.145 98	14.47 1	1456406 5.2
126	4-Methoxycinnamaldehyde	C10 H10 O2	-2.5	162.067 67	10.77 1	1449444 6.9
127	Guaiacol	C7 H8 O2	-0.66	124.052 35	9.207	1434320 1.65
128	Methyl linoleate	C19 H34 O2	-3.97	294.254 71	20.68 6	1421148 0.42
129	Eicosapentanoic acid	C20 H30 O2	-3.49	302.223 52	22.58	1420870 3.13
130	Nandrolone	C18 H26 O2	-2.76	274.192 52	14.80 7	1324336 7.08
131	(4E)-1-(4-Hydroxyphenyl)-4-decen-3-one	C16 H22 O2	-3	246.161 24	16.03 7	1247848 9.91
132	2-Methoxyresorcinol	C7 H8 O3	-3.01	140.046 92	9.645	1241162 3.58
133	7-Hydroxyflavan	C15 H14 O2	-2.89	226.098 73	11.65 3	1135984 3.24

134	4,8,12-trimethyltrideca 1,3,7,11-tetraene	C16 H26	-2.81	218.202 84	20.81 6	9897947 .401
135	Eicosapentanoic acid	C20 H30 O2	-3.49	302.223 52	22.17 3	8676767 .851
136	3-Methyl-2-butenyl caffeate	C14 H16 O4	-1.47	248.104 49	13.21 4	8511089 .247
137	Thymoquinone	C10 H12 O2	-1.6	164.083 47	12.50 5	8440170 .481
138	Isorhamnetin	C16 H12 O7	-2.22	316.057 6	14.84 3	8058961 .505
139	2-Octenoic acid	C8 H14 O2	-1.16	142.099 21	10.80 7	7572010 .605
140	1-(3,4-Dihydroxyphenyl)acetone	C9 H10 O3	-2.23	166.062 62	10.76	6400114 .457

Supplementary material 6

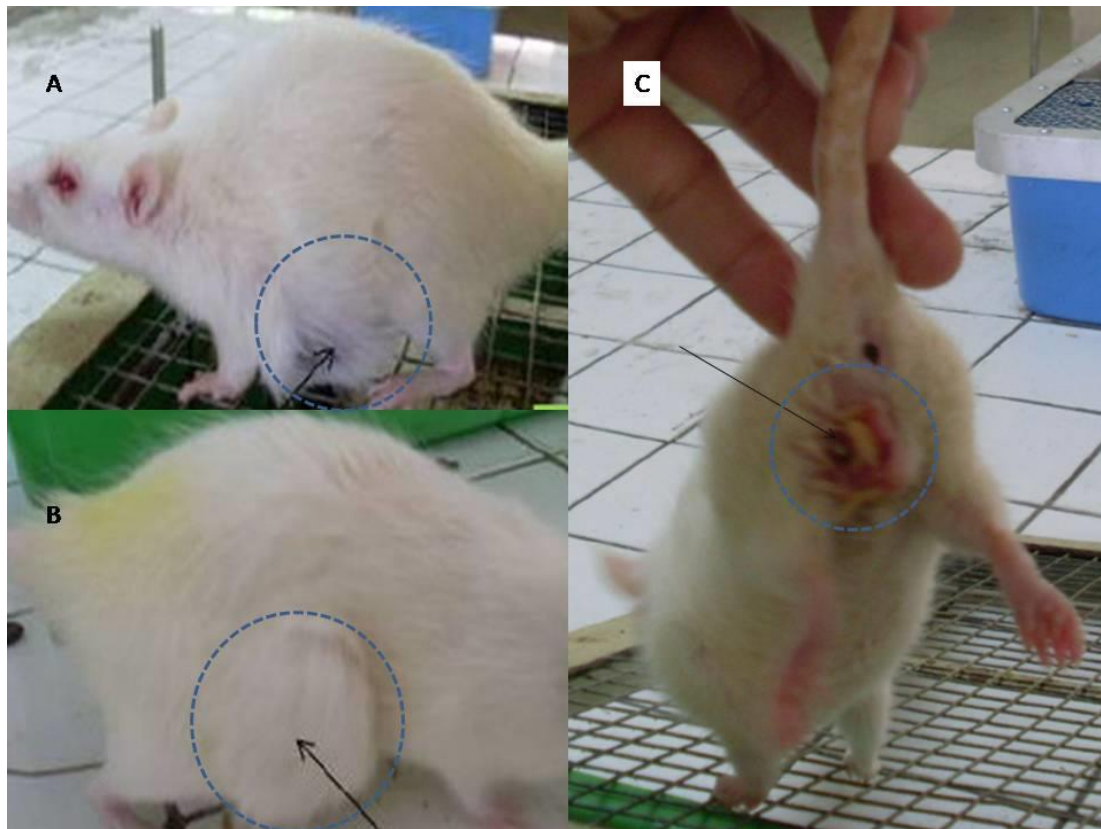


Figure 8. Nodules (arrows) were formed in the mammary gland in the 20th week of observation of SD rats after receiving CXBCH 2 weeks before and five weeks after DMBA induction. Nodules formed in all parts of the mammary gland (fore legs (A), near the hind legs (B), and some nodules break up (C). Note: Arrows indicate nodules