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Phytochemicals and bioactivities of *Anemone raddeana* Regel: a review

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Anemone raddeana, usually called as “Toujian Liang” in China, is an *Anemone* herb belonging to the Ranunculaceae family. Until now there are in total 67 of chemical components identified including triterpenoids, steroids, lactones, fats and oils, saccharide and alkaloids. A broad spectrum of pharmacological activity of *A. raddeana* compounds have been reported, such as antitumor, antimicrobial, anti-inflammatory, sedative and analgesic activities, as well as anti-convulsant and anti-histamine effects. In view of this, we initiated this short review to present the phytochemical and pharmacological profile of *A. raddeana* to support future studies in this discipline.

1. Introduction

Anemone raddeana Regel is a traditional Chinese medicinal herb belonging to the *Anemone* genus (Ranunculaceae), which is widely distributed in Russia (Far east), northeast of China, Japan and Korea (Chen et al. 2009). The aboveground parts and rhizome of *Anemone raddeana* are shown in Figs. 1 and 2. The rhizome of *A. raddeana* is usually used for the treatment of rheumatism, neuralgia, cancer and so on (Sun et al. 2009). Its main constituents include triterpenoids, steroids, lactones, fats and oils, saccharide and alkaloid. Extensive phytochemical and pharmacological studies on this plant proved triterpenoid saponins to be the main bioactive principles, and most of them



Fig. 1: Aerial parts of *Anemone raddeana*



Fig. 2: Rhizome of *Anemone raddeana*

are oleanane-type saponins (Sun and Liu 2008). In searching for bioactive natural products and to understand the underlying pharmacological mechanisms, the structure and biological activities of the chemical constituents of *A. raddeana* are described and presented in this review.

2. Chemical constituents

So far, 67 constituents are reported from the rhizome of *A. raddeana*. Most of them have been confirmed to be triterpenoid saponins. Their chemical structures are shown below (1–67) and their names, types and corresponding references

Table: Compounds from the rhizome of *Anemone raddeana*

No.	Compound name	References
<i>Triterpenoids</i>		
1	Oleanolic acid	Lu et al. (2001); Lu et al. (2002); Liu (1983c); Wu, Zhu. (1983a)
2	3-Acetyloleanolic acid	Lu et al. (2001); Lu et al. (2002)
3	Raddeanoside R ₀	Wu, Zhu. (1983a); Fan et al. (2010)
4	Raddeanoside R ₁	Wu, Zhu. (1985a); Wu, Zhu. (1983b)
5	Raddeanoside R ₂	Wu, Zhu. (1984a)
6	Raddeanoside R ₃	Wu, Zhu. (1983b); Wu, Zhu. (1984a); Kuang et al. (1996)
7	Raddeanoside R ₄	Wu, Zhu. (1983b); Wu, Zhu. (1984b); Wu, Zhu. (1984c)
8	Raddeanoside R ₅	Wu, Zhu. (1983b); Wu, Zhu. (1984b); Wu, Zhu. (1985b)
9	Raddeanoside R ₆	Wu, Zhu. (1984b); Wu, Zhu. (1984d)
10	Raddeanoside R ₇	Wu, Zhu. (1984b); Wu, Zhu. (1984d)
11	Raddeanoside R ₈	Kuang et al. (1996); Wu et al. (1989)
12	Raddeanoside R ₉	Wu et al. (1989)
13	Raddeanoside R ₁₀	Lu et al. (2001); Zhang et al. (1997)
14	Raddeanoside R ₁₁	Zhang et al. (1997)
15	Raddeanoside R ₁₂	Lu et al. (2001); Lue et al. (2002)
16	Raddeanoside R ₁₃	Lu et al. (2001); Lue et al. (2002)
17	Raddeanoside R ₁₄	Wang et al. (2004)
18	Raddeanoside R ₁₅	Wang et al. (2004)
19	Raddeanoside R ₁₆	Xia et al. (2004a)
20	Raddeanoside R ₁₇	Xia et al. (2004a)
21	Raddeanoside R ₁₈	Xia et al. (2004b)
22	Raddeanoside R _{19a}	Li et al. (2008)
23	Raddeanoside R _{19b}	Lu et al. (2009)
24	Raddeanoside R ₂₀	Chen et al. (2009); Lu et al. (2009)
25	Raddeanoside R ₂₁	Chen et al. (2009); Lu et al. (2009)
26	Raddeanoside R ₂₂	Fan et al. (2010b)
27	Raddeanoside R ₂₃	Fan et al. (2010b)
28	Raddeanoside R _a	Fan et al. (2010c)
29	Raddeanoside R _b	Fan et al. (2010c)
30	27-Hydroxyoleanolic acid 3-O-β-D-glucopyranosyl (1→2)-α-L-arabinopyranoside	Fan et al. (2010a)
31	3-O-α-L-rhamnopyranosyl (1→2) [β-D-glucopyranosyl (1→4)]-α-L-arabinopyranosyl-27-hydroxyoleanolic acid	Fan et al. (2010a)
32	28-O-α-L-rhamnopyranosyl (1→4)-β-D-glucopyranosyl (1→6)-β-D-glucopyranoside	Fan et al. (2010b)
33	Oleanolic acid 3-O-β-D-glucopyranosyl (1→4)-α-L-arabinopyranoside	Fan et al. (2010b)
34	Hederacholichiside E (Hederacolchiside E)	Fan et al. (2010b); Chen et al. (2009)
35	Hederasaponin B (Hederagenin B)	Fan et al. (2010b); Kuang et al. (1996); Wang et al. (2004); Chen et al. (2009)
36	Eletheroside K (Eleutheroside K)	Chen et al. (2009); Lu et al. (2002); Kuang et al. (1996)
37	Leonloside D	Xia et al. (2004b)
38	Hederacholichiside F	Xia et al. (2004b)
39	Lupeol	Yamashita et al. (2002)
40	Betulin	Lu et al. (2002); Yamashita et al. (2002)
41	Betulinic acid	Lu et al. (2002); Yamashita et al. (2002)
<i>Steroids</i>		
42	Diosgenin	Lu et al. (2002); Wu, Zhu. (1983a)
<i>Lactones</i>		
43	Protoanemonin	Liu (1983a)
44	Ranunculin	Liu (1983a)
45	Anemonin	Liu (1983b)
<i>Fats and oils</i>		
46	2-Pentyl-furan	Liu et al. (1984)
47	6-Methyl-1-heptand	Liu et al. (1984)
48	Hexanoic acid	Liu et al. (1984)
49	Patchoulene	Liu et al. (1984)
50	2-methyl-tetradecane	Liu et al. (1984)
51	2,6-Di-tert-butyl-4-methylphenol	Liu et al. (1984)
52	N-Hexadecane	Liu et al. (1984)
53	5-Ethyl-5n-propylundecane	Liu et al. (1984)
54	2-Methylhexadecane	Liu et al. (1984)
55	2,6,10,14-Tetramethyl hexadecane	Liu et al. (1984)
56	Ethyl palmitate	Liu et al. (1984)

Table: (Continued)

No.	Compound name	References
56	N-butyl isobutyl phthalate	Liu et al. (1984)
57	Linoleic acid	Liu et al. (1984); Liu et al. (2003)
58	Phenylacetaldehyde	Liu et al. (1984)
59	Phenethyl alcohol	Liu et al. (1984)
60	α -Terpineol	Liu et al. (1984)
61	P-tert-Butylphenetole	Liu et al. (1984)
62	4-Hydroxy-3-methoxyacetophenone	Liu et al. (1984)
63	7,9-di-Methyl-hexadecane	Liu et al. (1984)
64	Nonadecanol	Liu et al. (1984)
<i>Others</i>		
65	Glucose	Wu, Zhu. (1985a)
66	Sucrose	Wu, Zhu. (1985a)
67	evonymitol	Lu et al. (2002)

are listed in the Table. These compounds include triterpenoids (1–40), steroids (41), lactones (42–44), fats and oils (45–64), and others (65–67).

2.1. Triterpenoids

Triterpenes consist of 6 isoprene units, and are an important class of chemical components in Chinese medicine. Most triterpenoids, like compound 1–35, isolated from the rhizome of *A. raddeana* are oleanane derivatives, namely oleanane-type saponins, which are the major components of this plant. Normally they are monodesmosides and bisdesmosides composed of a molecule of oleanolic acid and 1–9 molecules of saccharide ligands, such as glucose, arabinose and rhamnose. However in 2004, Xia et al. identified two hederagenin-derived saponins from the rhizome of *A. raddeana*, namely leonloside D (36) and hederacholichiside F (37), which are all composed of a molecule of hederagenin and 1–3 molecules of rhamnose, glucose, or arabinose. Compounds 38–40 belong to the lupane-type triterpenoids (Lu et al. 2004; Yamashita et al. 2002).

2.2. Steroids

Wu and Zhu (1983) firstly isolated and identified compound 41 (Diosgenin) from the rhizome of *A. raddeana*. Lu et al. (2002) once more reported this component. Up to now this is the only steroid found in *A. raddeana*.

2.3. Lactones

Liu (1983a) firstly reported the isolation of compound 42 (Protoanemonin) and 43 (Ranunculin), respectively. And then compound 44 (Anemonin) was identified (Liu 1983b).

2.4. Fats and oils

Liu et al. (1984) make use of steam distillation and ether extraction methods to obtain volatile substances from the rhizome of *A. raddeana*, namely fats and oils. And then these components (Compound 45–64) were isolated and identified by gas chromatography combined with mass spectrometry (GC/MS) (Liu et al. 2003).

2.5. Others

Glucose (65) and sucrose (66) were confirmed present in *A. raddeana* by Wu and Zhu (1985a). Evonymitol (67) was identified by Lu et al. (2002).

3. Pharmacological research

3.1. Antitumor activity

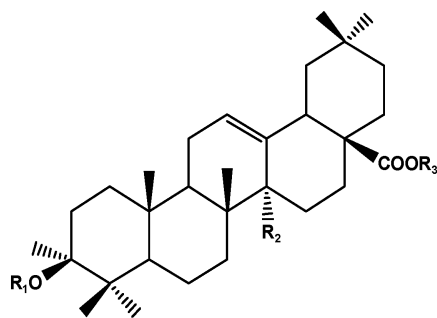
Wang et al. (2008a) evaluated *in vitro* and *in vivo* the antitumor activity of crude saponins from the rhizome of *A. raddeana*. The inhibition on KB, HCT-8, MCF-7WT and MCF-7/ADR cells was measured with MTT *in vitro*, and the 50% inhibition concentration (IC₅₀) was 7.68, 18.52, 17.34 and 19.43 μ g/mL respectively. The *in vivo* inhibition on tumor S₁₈₀, liver cancer H₂₂ and EAC mice was 68.1%, 62.5% and 69.3%, respectively. The results indicated that the crude saponins prepared in this way had good inhibitory activity on tumors *in vitro* and *in vivo*, and showed some potential as anti-cancer medicines. At the same time, Wang et al. (2008b) also stated that the purified constituent raddeanoside R₃ has good antitumor activity both *in vitro* and *in vivo*. Ren et al. (2005) found that raddeanoside R₂, raddeanoside R₃, eleatheroside K and hederasaponin B showed a very strong inhibitory effect on human gastric cancer cell line BGC823 and human leukemia cell line K562 in a dose-dependent manner. The antitumor activity of crude saponins, raddeanoside R₂ and raddeanoside R₃ was related to their structural features. Depending on IC₅₀ values, the effective inhibition sequence was crude saponins > raddeanoside R₂ > raddeanoside R₃. There exists some regularity and synergistic effect among the three constituents, a compound with a longer sugar chain is less effective, and the mixture is the most effective (Zhang et al. 2003).

3.2. Antimicrobial activity

Liu (1988) reported that volatile oil, lactones, and saponins from the rhizome of *A. raddeana* exhibit varying degrees of inhibition effect on human pathogenic Streptococci, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Shigella*, and *Staphylococcus aureus*. *In vitro*, anemonin showed antifungal activity, with a minimum inhibitory concentration of 15 μ g/ml (Zhou et al. 2007).

3.3. Anti-inflammatory activity

Crude saponins from the rhizome of *A. raddeana* have a suppression effect on rat paw edema induced by carrageenan, formaldehyde and dextran. Among these three groups, crude saponins showed the strongest inhibitory effect on the group treated by formaldehyde. Furthermore raddeanoside R₁ significantly depressed the swelling caused by carrageenan, and the intensity was higher than that of crude saponins (Wang et al. 1985).



	R1	R2	R3
1	H	CH3	H
2	Ac	CH3	H
3	α -L-Ara	CH3	H
4	α -L-Rha (1→4)- α -L-Ara	CH3	H
5	β -D-Glc (1→2)- α -L-Ara	CH3	H
6	α -L-Rha (1→2)- β -D-Glc (1→2)- α -L-Ara	CH3	H
7	α -L-Rha (1→4)- α -L-Ara	CH3	α -L-Rha (1→2)- β -D-Glc
8	α -L-Rha (1→2)- β -D-Glc (1→2)- α -L-Ara	CH3	α -L-Rha (1→4)- β -D-Glc
9	β -D-Glc (1→2)- α -L-Rha (1→4)- α -L-Ara	CH3	H
10	β -D-Glc (1→2)- α -L-Ara	CH3	α -L-Rha (1→4)- β -D-Glc
11	α -L-Rha (1→2)- β -D-Glc (1→2)- α -L-Ara	CH3	α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
12	α -L-Rha (1→2)- β -D-Glc (1→2)- α -L-Ara	CH2OH	α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
13	α -L-Rha (1→2)- β -D-Glc (1→2)- α -L-Ara	CH3	α -D-Glc (1→3)- α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
14	α -L-Rha (1→2)- β -D-Glc (1→2)- α -L-Rha	CH3	β -D-Glc (1→6)- α -D-Glc (1→3)- α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
15	α -L-Rha (1→2)- α -L-Ara	CH2OH	H
16	α -L-Rha (1→2)-[β -D-Glc (1→4)]- α -L-Ara	CH3	H
17	α -L-Rha (1→2)-[β -D-Glc (1→4)]- α -L-Ara	CH3	β -D-Glc (1→6)- β -D-Glc
18	α -L-Ara (1→3)- α -L-Rha (1→2)- α -L-Ara	CH3	α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
19	α -L-Ara (1→3)- α -L-Rha (1→2)-[β -D-Glc (1→4)]- α -L-Ara	CH3	α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc

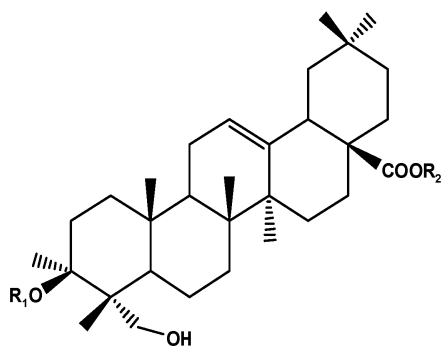
Anti-inflammatory activity and inhibition of neutrophil peroxide production are closely associated with each other. The effect of six compounds isolated from the rhizome of *A. raddeana* on the superoxide generation in human neutrophils was investigated by Lu et al. (2001). The six compounds examined were oleanolic acid, 3-acetyloleanolic acid, eletheroside K, raddeanoside R₁₀, raddeanoside R₁₂, and raddeanoside R₁₃. The results showed that in most cases the compounds can suppress superoxide generation induced by phorbol 12-myristate 13-acetate (PMA), N-formyl-methionyl-leucylphenylalanine (fMLP), and arachidonic acid. Occasionally some constituents enhance or weakly suppress the superoxide generation. Thereafter they have found that various compounds affected the stimulus induced superoxide generation in parallel to tyrosyl phosphorylation of neutrophil proteins in

human neutrophils (Chen et al. 2009). Yamashita et al. (2002) also reported that lupeol and betulin suppress superoxide generation by preventing tyrosyl phosphorylation of a 45.0-kDa protein in human neutrophils.

3.4. Sedative and analgesic activity

Crude saponins, raddeanoside R₁ and other two unconfirmed constituents raddeanoside F and raddeanoside H from the rhizome of *A. raddeana* had analgesic effect to pain reaction in mice induced by acetic acid. However, at a dose of 125 mg/kg raddeanoside F and raddeanoside H were not effective. Spontaneous activity of mice could be suppressed by crude saponins and rad-

	R1	R2	R3
20	β -D-Glc (1→4)- β -D-Glc (1→3)- α -L-Rha (1→2)- α -L-Ara	CH3	α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
21	β -D-Glc (1→2)-[β -D-Glc (1→4)]- α -L-Ara	CH3	α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
22	α -L-Rha (1→2)- β -D-Glc (1→2)- α -L-Ara	CH3	α -L-Rha (1→4)- β -D-Glc (1→6)- α -D-Glc (1→3)- α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc (1→3)- α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
23	β -D-Glc (1→4)- α -L-Ara	CH3	α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
24	α -L-Rha (1→2)-[β -D-Glc (1→4)]- α -L-Ara	CH2OH	H
25	α -L-Rha (1→2)- α -L-Ara	CH2OH	α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
26	β -D-Glc (1→2)-[β -D-Glc (1→4)]- α -L-Ara	CH3	H
27	α -L-Ara (1→3)- α -L-Rha (1→2)-[β -D-Glc (1→4)]- α -L-Ara	CH3	H
28	β -D-Glc (1→4)- α -L-Ara	CH2OH	H
29	α -L-Ara (1→3)- α -L-Rha (1→2)- α -L-Ara	CH2OH	H
30	β -D-Glc (1→2)- α -L-Ara	CH2OH	H
31	α -L-Rha (1→2)-[β -D-Glc (1→4)]- α -L-Ara	CH2OH	α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
32	β -D-Glc (1→4)- α -L-Ara	CH3	H
33	α -L-Rha (1→2)-[β -D-Glc (1→4)]- α -L-Ara	CH3	α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
34	α -L-Rha (1→2)- α -L-Ara	CH3	α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
35	α -L-Rha (1→2)- α -L-Ara	CH3	H



- 36 R₁= β -D-Glc (1→4)- α -L-Ara R₂= α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc
- 37 R₁= α -L-Rha (1→2)-[β -D-Glc (1→4)]- α -L-Ara R₂= α -L-Rha (1→4)- β -D-Glc (1→6)- β -D-Glc

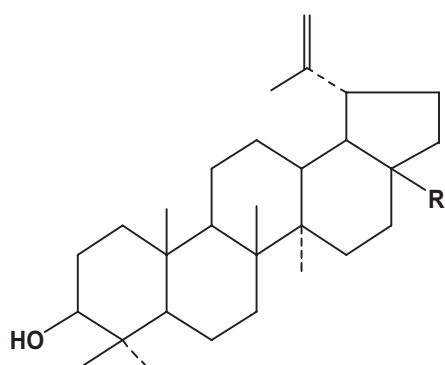
deanoside R₁, and the latter was more potent. Protoanemonin also had a calming effect (Wang et al. 1985).

3.5. Anti-convulsant and anti-histamine activity

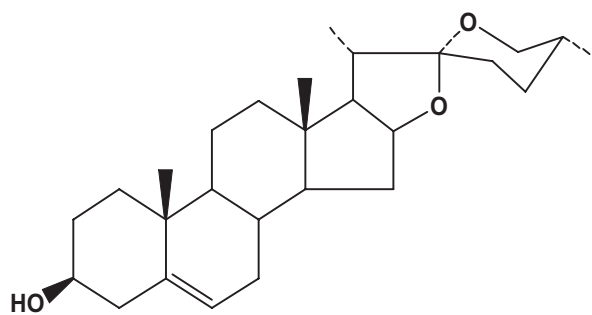
Crude saponins from the rhizome of *A. raddeana* influenced convulsions in mice induced by strychnine, but had no effect on mice convulsions induced by theine. Protoanemonin was effective against bronchospasm induced by 0.01% histamine, which also resist to the contraction of isolated ileum from guinea pig induced by histamine (Wang et al. 1985).

4. Conclusion

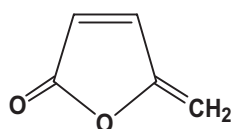
The phytochemical investigations on the rhizome of *A. raddeana* revealed the occurrence of a wide range of chemical compounds including triterpenoids, steroids, lactones, fats and oils, as well as other constituents. Out of the 67 different components described in the present review 40 belong to the groups of triterpenoid saponins and triterpenoids mostly oleanane-type saponins known to be bioactive. Nevertheless, there are still many constituents that have received no or only little attention so far, therefore more phytochemical and biological studies should be focused on these constituents. To

38 R=CH₃39 R=CH₂OH

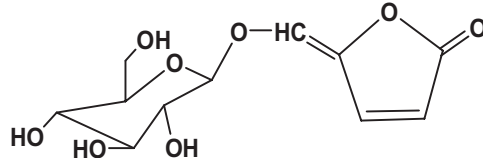
40 R=COOH



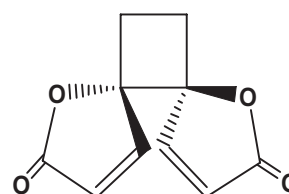
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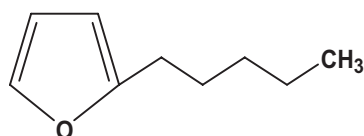
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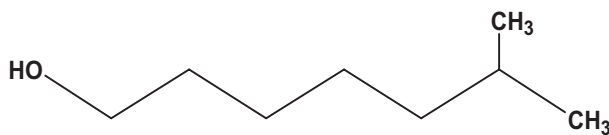
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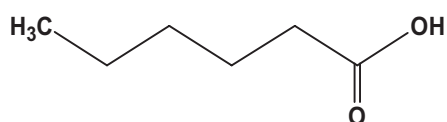
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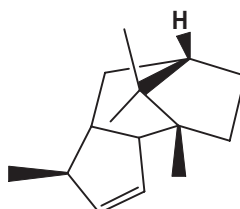
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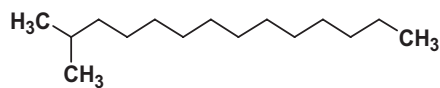
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search for more potential bioactive components, further phytochemical and biological-activity studies on this plant are required.

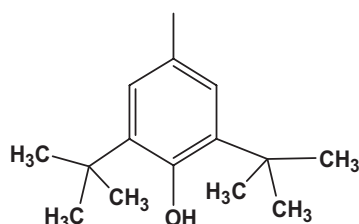
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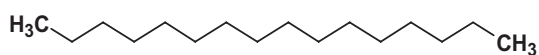
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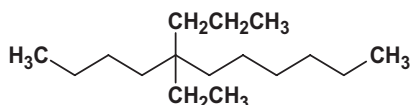
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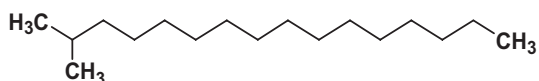
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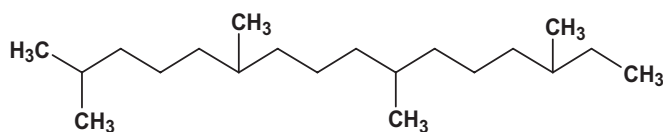
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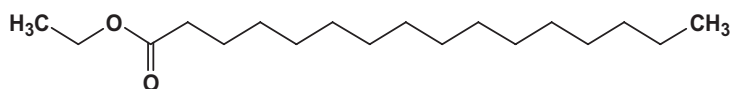
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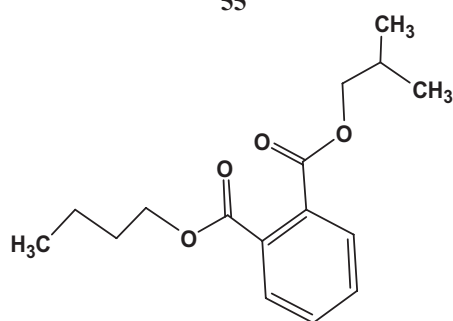
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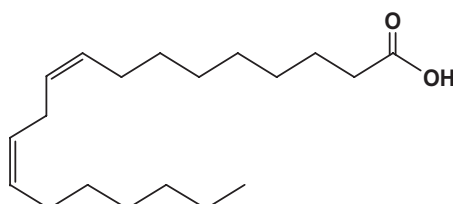
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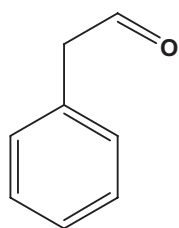
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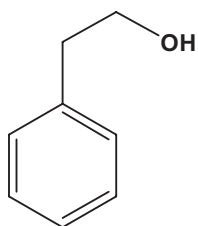
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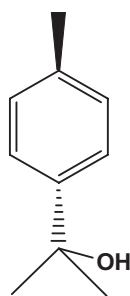
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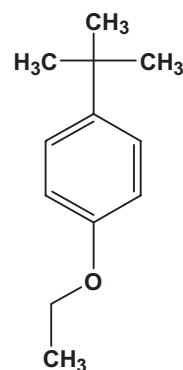
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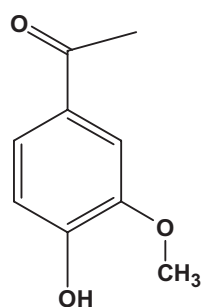
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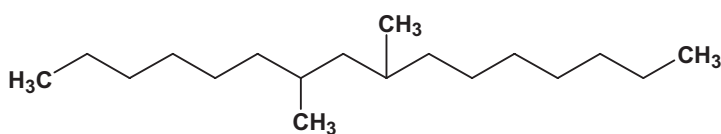
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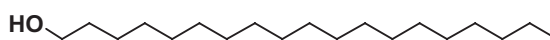
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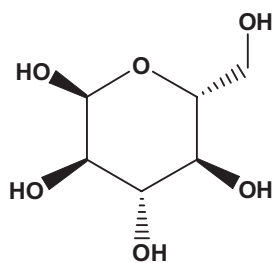
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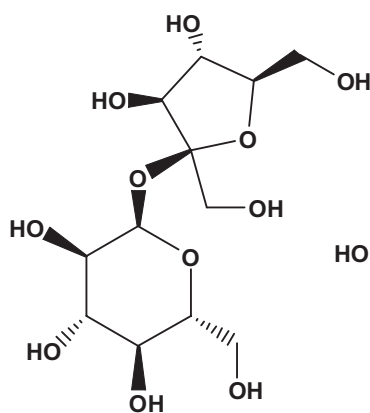
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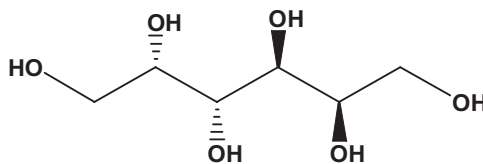
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