10

Synthesis and Medicinal Uses of Sesquiterpenoids and Sesterpenoids

Biswa Mohan Sahoo*, Bimal Krishna Banik†, and Abhishek Tiwari‡

DOI: 10.1201/9781003008682-10

CONTENTS

10.1 Introduction

Sesquiterpenes (C_{15} terpenoids) are the class of terpenes which consist of three isoprene units. Plant families, known to be principal producers of sesquiterpene volatiles, include Lamiaceae, Geraniaceae, Rutaceae, Myrtaceae, Asteraceae, Cannabaceae and Gingeraceae. A number of highly functionalized, nonvolatile sesquiterpenes of plant origin have demonstrated highly specific biological activity and have therefore been investigated for their clinical potential. Examples of sesquiterpene include α-Zingiberene (*Zingiber officinalis*), α-Farnesene (*Eucalyptus globules*) [1, 2, 3].

Another class of compounds contains various characteristic features such as α-methylene γ-lactone system, α, β-unsaturated carbonyls and epoxides. These are chemically distinct from the sesquiterpenoids and are collectively known as sesquiterpenoid lactones (Figure 10.1). The specific and vital nucleophiles present in the enzyme system such as thiol and amino moieties help to augment faster and reactive approach toward receptor sites by these sesquiterpenoid lactones. Thus, these compounds exhibit marked and pronounced biological activities such as anti-inflammatory, antimicrobial, antioxidant, antitumor and antimalarial. Examples of sesquiterpene lactone include Tenulin (*Helenium amarum*), Thapsigargin (*Thapsia garganica*), Artemisinin (*Artemisia annua*), Germacranolide (*Geranium macrorrhizum*), Eudesmanolide (*Magnolia obovata*), Matricarin (*Achillea vermacularis*) and Guaianolide (*Guaiacum officinale*) [4].

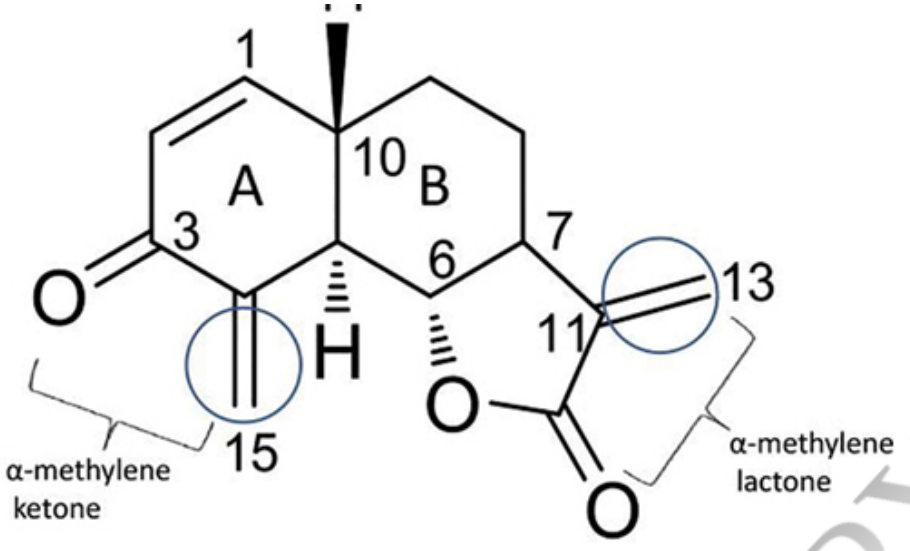


FIGURE 10.1 Structure of sesquiterpenoid lactones.

Sesquiterpenols possess fifteen carbon atoms (C_{15}) in their structure and exhibit diverse therapeutic effects such as antifungal, antiviral, antinociceptive, insecticidal, analgesic and anti-inflammatory. Sesquiterpenols are derived from Sesquiterpenes by addition of hydroxyl (-OH) group. Examples: Farnesol (*Santalum spicatum)*, α-Bisabolol (*Matricaria recutita*), Patchoulol (*patchouli cablin*) and Nerolidol (*Melaleuca quinquenervia*) [5].

* Roland Institute of Pharmaceutical Sciences, Berhampur affiliated to Biju Patnaik University of Technology (BPUT), Rourkela, Odisha, India. Corresponding author e-mail address: drbiswamohansahoo@gmail.com.

† Department of Mathematics and Natural Sciences, College of Sciences and Human Studies, Prince Mohammad Bin Fahd University, Al Khobar, Kingdom of Saudi Arabia. Corresponding author e-mail address: bimalbanik10@gmail.com.

‡ Faculty of Pharmacy, Pharmacy Academy, IFTM University, Lodhipur Rajput, Moradabad-244102, Uttar Pradesh, India.

Sesterpenes (C_{25} terpenoids) are the class of terpenes which consist of five isoprene units with molecular formula $C_{25}H_{40}$. Sesterpenes and their derivatives are collectively known as sesterterpenoids. These are ubiquitous secondary metabolites in fungi, marine organisms and plants. Their structural diversity includes carbotricyclic ophiobolanes, polycyclic anthracenones, polycyclic furan-2-ones and polycyclic hydroquinones. Examples of sesterterpenoids include Merochlorin-A (*Streptomyces sp.*), Ophiobolin-A (*Drechslera gigantean*), Secoemestrin-D (*Emericella sp.*), Manoalide (*Luffariella variabilis*), Luffariellolide (*Luffariella sp.*), Hippolide-A (*Hippospongia lachne*), Palauolol (*Thorectandra sp.*), Kohamaic acid-A (*Ircinia spp.*) and Petrosaspongiolides (*Petrosaspongia nigra*). Furthermore, most of them possess promising biological activities such as antibacterial, antifungal, anti-inflammatory, antioxidant and cytotoxicity [6].

10.1.1 Classification of Sesquiterpenoids

Sesquiterpenoids are categorized into four classes such as acyclic, monocyclic, bicyclic and tricyclic, as summarized in Table 10.1. Examples include α-Farnesene (*Eucalyptus globules*), α-bisabolene in black pepper (*Piper nigrum*) and β-caryophyllene in ylang ylang (*Cananga odorata*) and Santalene (*Santalum album*) (Table 10.2) [7,8].

TABLE 10.1

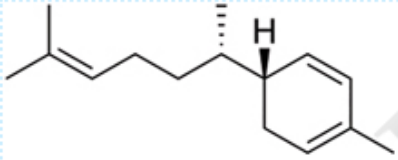
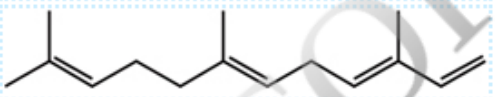
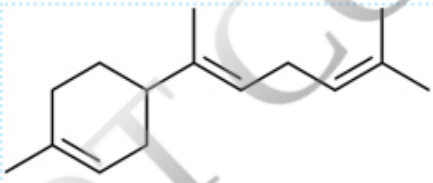
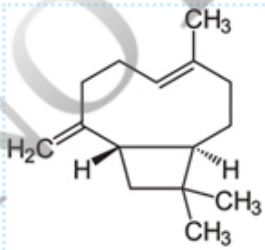
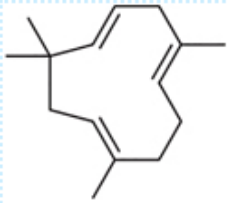
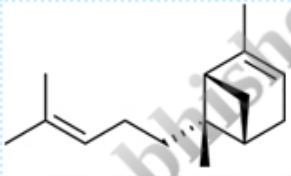
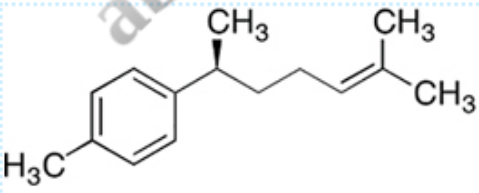
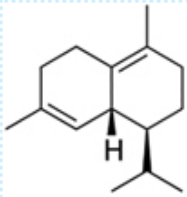
Classification of Sesquiterpenoids

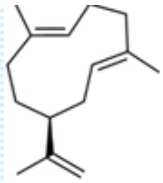
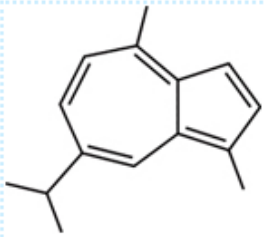
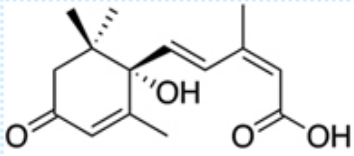
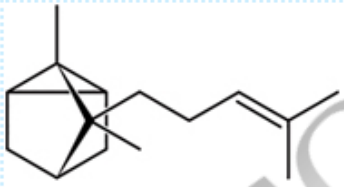
Types of Sesquiterpenes	Name of Sesquiterpenes
Acyclic	α-Farnesene β-Farnesene
Monocyclic	Abscisic acid α-Bisabolene *α-Curcumene* Humulene α-Zingiberene
	α-Bergamotene

Bicyclic	β-caryophyllene Cadinene Germacrene-A Guaiazulene
Tricyclic	Santalene

TABLE 10.2

List of Sesquiterpenoids and Their Biological Properties

Sesquiterpenes	Biological Source	Structure	Biological Properties
α-Zingiberene	*Zingiber officinalis*		Antioxidant, increases glutathione production and reduces inflammation
α-Farnesene	*Eucalyptus globulus*		Effective against cariogenic bacteria that cause tooth decay
α-Bisabolene	*Piper nigrum*		Acts as pheromones in different insects
β-Caryophyllene	*Cananga odorata*		Anti-toothache
Humulene	*Humulus lupulus*		Anti-inflammatory
α-Bergamotene	*Citrus bergamia*		Anti-inflammatory
α-Curcumene	*Curcuma longa*		Anti-inflammatory
δ-Cadinene	*Juniperuscommunis*		Antioxidant

Germacrene-A	*Lamium purpureum*		Antimicrobial and insecticidal
Guaiazulene	*Oil of guaiac and chamomile oil*		Component of skin care products
Abscisic acid	*Lemon, Avocado*		Plant growth hormone
Santalene	*Sandalwood oil*		Flavor and fragrance agent

10.1.2 Biosynthesis of Sesquiterpene

Sesquiterpenes are derived from farnesyl diphosphate (FDP) and can be cyclized to produce diverse chemical structures. The reaction of geranyl pyrophosphate with isopentenyl pyrophosphate results in the 15-carbon farnesyl pyrophosphate (FPP) (Figure 10.2), which is an intermediate in the biosynthesis of sesquiterpenes such as farnesene [9].

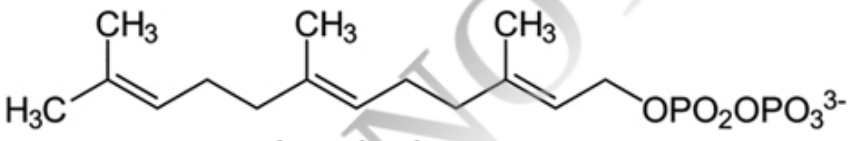


FIGURE 10.2 Farnesyl pyrophosphate.