1 Introduction to Chamomile

1.1 INTRODUCTION

Chamomile (*Matricaria recutita* L.), commonly known as German chamomile, is an important medicinal and aromatic plant. The plant belongs to the daisy (Asteraceae) family and the flowers have a characteristic herbaceous fragrance. The flowers are actually not individual flowers but inflorescences. Throughout this book, the word *flowers* would be used to denote the *inflorescences* or *capitula*.

The name *Chamomile* is derived from two Greek words: *Khamai* meaning "on the ground" and *melon* meaning "apple." Pliny the Elder mentioned that the plant has an apple-like smell (Franke 2005), and the name is attributed to the Roman chamomile, the flowers of which have an apple-like aroma (Hanrahan and Frey 2005; The Columbia Encyclopedia 2012). The Roman chamomile (*Chamaemelum nobile* [L.], earlier known as *Anthemis nobilis* [L.]), also belongs to the family Asteraceae and looks similar to the German chamomile. However, there are morphological differences between the flowers of the Roman and German chamomile. Further, the essential oil and chemical constituents of German chamomile and Roman chamomile are markedly different (Mann and Staba 1986). Consequently, their properties and uses are quite different. Therefore, the knowledge of the differences between Roman and German chamomile is useful. However, the discussion of Roman chamomile is beyond the scope of this book as it deals exclusively with the German chamomile and henceforth, the name "chamomile" will be used to denote German chamomile throughout the book.

Chamomile is commonly known by different names all over the world, such as chamomile, flos chamomillae, German chamomile, Hungarian chamomile, *Matricaria* flowers, pinheads, sweet false chamomile, true chamomile, wild chamomile, and Babuna (WHO 1999). Carl Linnaeus made the earliest attempt to systematically classify chamomile and give it the botanical name—*Matricaria*. The name *Matricaria* was chosen by Linnaeus perhaps due to its wide use in treating gynecological diseases, or "diseases of the womb (matrix)" (Franke 2005). The species name attributed by Linnaeus in 1753 (Linnæi 1753) came into controversy and since then, several taxonomists have been working on the correct nomenclature of chamomile.

Chamomile originated in Europe and West Asia (Bisset 1994) and since ancient times, it has been highly valued by the Egyptians, Romans, and Greeks for its medicinal properties. The Egyptians considered the plant sacred and believed it was a gift from the God of the Sun (Salamon 1993). The Saxons considered chamomile as one of the nine sacred herbs and the Egyptians dedicated the plant to the sun god Ra

(Hanrahan and Frey 2005). It is revered so highly in Slovakia that there is a saying that one must bow to the chamomile plant if one comes across it (Salamon 2004, 2007).

It has been used since the time of Hippocrates, the father of medicine, in 500 BCE. The ancient Greeks, Egyptians, and Romans regularly used the chamomile flowers to treat erythema and xerosis caused because of dry weather (Baumann 2007) and as a calming beverage in the form of tea or tisane (Lissandrello 2008). Several eminent scientists of ancient times, such as Hippocrates, Pliny, Dioscorides, Galen, and Asclepiades studied the plant and passed on their knowledge to the subsequent generations through their writings (Salamon 1993). Hippocrates described chamomile as a medicinal plant and chamomile tea was recommended by Galen and Asclepiades (Carle and Gomma 1991/92). During the same period, Mathiolus/Peter Ondej Mathioli described chamomile in his Latin herbarium (Salamon 1993), where he listed the essential oil of chamomile as a remedy against spasms (Carle and Gomaa 1991/92).

Chamomile came into widespread use during the medieval age. It was extensively prescribed by the doctors of the sixteenth and seventeenth centuries for intermittent fevers (Antonielli 1928, as cited in Singh et al. 2011). In 1593, Bock described that chamomile flowers were used in all kinds of medicines and in 1664, Tabernaemontanus reported that chamomile was used in medicine in the form of plasters, ointments, pouches, and medicinal baths. In 1488, Saladin von Asculum described the blue oil of chamomile for the first time. In 1500, Heironimus Brunschwig described the distillation of chamomile oil (Franke 2005).

The chamomile flowers, on hydrodistillation, yield a blue oil that finds extensive use in medicines, cosmetics, and foodstuff. An extract of flowers is also prepared using water, alcohol, and various other solvents. The essential oil and flower extracts contain about more than 120 secondary metabolites, such as chamazulene, (–)-α-bisabolol, apigenin, and luteolin, and many of these are pharmacologically active. Some of these compounds in the essential oil and the extracts are also used in perfumery and flavoring. The flower extract and essential oil possess anti-inflammatory (Al-Hindawi et al. 1989; Carle 1990; Carle and Gomma 1991/92) spasmolytic, carminative, antiseptic (Chetvernya 1986), sedative (Fundario and Cassone 1980), and ulcer protecting (Zaidi et al. 2012) properties. The flower extracts and the essential oil are therefore the ingredients of several folk and traditional herbal remedies, and other complementary and alternative systems of medicine (CAM), such as Homeopathy and Unani. Today, the ethnobotanical knowledge and use of chamomile is extensive and worldwide. It is evident through many studies carried out to explore its use as folk remedies.

Smitherman et al. (2005) studied the use of chamomile as folk remedies among urban African-American community in Michigan. They found that the knowledge of folk remedies existed in the community and was used extensively by the caregivers. They also found that chamomile tea for treating colic was practiced by the caregivers. Zucchi et al. (2013) carried out an ethnobotanical survey on the use of chamomile in Ipameri, Brazil. They found that chamomile was one of the most used plants for medicinal purposes. Šavikin et al. (2013) found in an ethnobotanical study that in southwestern Serbia, chamomile was one of the most commonly

used plants for medicinal purposes. Raal et al. (2013) reported that in Estonia, chamomile flowers were frequently used as a self-medication to treat cold and flu. Malik et al. (2013) reported the increasing use of chamomile in homeopathy in Pakistan.

Traditionally, chamomile flowers have been handpicked and used. Gradually, the plants were cultivated for use. Chamomile has been said to be brought into cultivation during the Neolithic period approximately from 9000 to 7000 BC (Salamon 1993). However, the yield of these cultivated plants was low in terms of flowers, oil content, and oil quality. To develop high-yielding varieties, the first attempts in breeding were made a little over 50 years ago (Franke and Schilcher 2007). Several high-yielding varieties were developed, such as Manzana, Degumille, Bodegold, Zloty Lan, Bona, and Goral. Today, chamomile cultivation and use has spread to almost all parts of the world, and the chief producers of chamomile are Argentina, Egypt, Germany, France, Italy, Turkey, Greece, Bulgaria, Yugoslavia, Hungary, Slovakia, and Australia. It was estimated that in 2003, about 50,000 acres were under chamomile cultivation worldwide (Brester et al. 2003).

The worldwide demand and consumption of chamomile is high. The annual consumption of chamomile flowers in Germany alone in 1992 was reported to be about 5000 t (Franz 1992). In Australia, the demand is estimated to be above 50 t (Purbrick and Blessing 2007). In Italy, the demand for chamomile amounts to 1000–1200 t annually, worth €3 million (CBI Ministry of Foreign Affairs 2011). With the increasing use of chamomile formulations in herbal medicines and homeopathy and their increased availability as the over-the-counter drugs, the demand for chamomile is increasing in the South American countries such as Brazil (Freitas et al. 2012), Colombia (Gómez-Estrada et al. 2011), Chile (Burgos and Morales 2010), and Peru (Huamantupa et al. 2011). As the demand for chamomile-based products is increasing, countries such as India and Tasmania (Falzari et al. 2007) are planning to take up chamomile cultivation in a big way.

Considering the over-the-counter availability of chamomile-based drugs and increasing self-medication, the quality, safety, and efficacy of these drugs have achieved paramount importance. Needless to say, there are several issues in the quality, safety, and efficacy of the drugs. These issues are discussed in Sections 1.5.1.7, 1.5.2.4, and 1.5.3.4.

Chamomile flower extracts and oil are being used not only in medicinal formulations and aromatherapy (Buchbauer 1996), but also as foodstuffs for flavoring, in cosmetics (Mann and Staba 1986), cosmeceuticals (Thornfeldt 2005; Baumann 2007; Padma Preetha and Karthika 2009), and dyeing (Çaliş and Yücel 2009). Further, new uses of chamomile have been discovered in diverse areas, such as insect and pest repellence, veterinary, and reclamation of polluted soils. With such evidence, chamomile has proved to be a very important plant for the betterment of our society.

1.2 CHAMOMILE AS FOOD

The chamomile flowers are taken as tea, tisane, and herb beer (Chamomile 2006; McKay and Blumberg 2006). In fact, chamomile tea is one of the most popular herbal teas of the world and almost a million cups are consumed every day

(Srivastava et al. 2010). In addition to tea, the fresh flowers of chamomile can be taken as salads and drinks. The dried flowers can be used as an ingredient in soups and salads to improve the flavor and enhance the nutritional value. Drinks made from chamomile flowers such as chamomile lemonade could be a refreshing drink in summer (Lissandrello 2008).

Not only the whole flowers, but also the essential oil and the extract of the flowers are used in food. The aqueous ethanol extract of chamomile flowers can contain up to 20% of the original dry matter, including 20%–25% of the mineral components and 5% of the free amino acids. It can be added to all kinds of foodstuffs and drinks. Chamomile flower extracts and oil are used to render the characteristic flavor (Furia and Bellanca 1975; Gasič et al. 1989) to the items of food, confectionery, alcoholic and nonalcoholic beverages, and tobacco. Chamomile oil is used for coloring foods as well (Mann and Staba 1986; Emongor et al. 1990).

Because the essential oil of chamomile is antimicrobial, it can used as a coating on various food products (Aliheidari et al. 2013).

1.3 CHAMOMILE AS A COSMETIC INGREDIENT

Various preparations of chamomile based on the whole plant or flower extracts, oil of flower, and compounds isolated from chamomile find uses in cosmetic industries. A variety of skin and hair care preparations contain chamomile flower extracts or oil. The natural antioxidant and antimicrobial effects of chamomile oil renders it a safe cosmetic without any side effects (Khaki et al. 2012). Mouthwashes and toothpastes are also made using chamomile (Laksmi et al. 2011; Nimbekar et al. 2012). Chamomile oil is blended with other essential oils in certain perfumes. The kinds of cosmetics that contain chamomile are creams, ointments, shampoos, soaps, detergents, and perfumes (Mann and Staba 1986).

1.4 OTHER USES OF CHAMOMILE

Chamomile extracts have also found several other uses, such as for mosquito repellence (Thorsell et al. 1970; Thorsell 1988), biological control of pests (Barakat et al. 1985; Mishra 1990), dyeing (Çaliş and Yücel 2009), improvement of dairy (Abou Ayana and Gamal El Deen 2011), poultry (Poráčová et al. 2007), and veterinary medicine (Tilford 2004).

The chamomile plant is known for reclamation of sodic soils (Singh 1970) and bioremediation for metals such as cadmium (Chand et al. 2012).

1.5 MEDICINAL USES OF CHAMOMILE

Chamomile is used for medicinal purposes in the traditional system of medicine, homeopathy, and Unani system of medicine. These three systems of medicine are referred to as CAM. These systems use chamomile in specific disease conditions. These systems of medicine have their own unique way of preparing the distinct drug formulations and dispensing them. Each system markets different kinds of drugs.

1.5.1 Use of Chamomile in the Traditional System of Medicine

The use of chamomile for medicinal purposes in the traditional system of medicine is mostly guided by the pharmacopoeias. The pharmacopoeias are authoritative texts that specify how to identify the correct plant, which plant part is to be used, what physical and chemical qualities of the drug are required, and how the drug formulations should be prepared and administered to the patient. These specifications ensure that the drug is effective. In addition to the pharmacopoeias, there are other authoritative texts such as compendiums and monographs that provide guidance on the effective formulations and use of chamomile.

The chamomile flowers used as whole flowers or extracts in alcohol or water are made from the dried flowers. The essential oil of the flower is also used. The whole flowers are used as teas, tinctures, tablets, and compresses. The guidelines in many of the pharmacopoeias specify that the flowers used for medicinal purposes should have a minimum of 0.4% volatile oil content (Schilcher 2005a). The hydroalcoholic extracts of the flowers and the hydrodistilled essential oils are used in creams, lotions, and aromatherapy. The teas, tinctures, and extracts are prepared according to prescribed specifications.

1.5.1.1 Preparation of Tea

Chamomile tea, as described by the German Commission E monograph, is prepared by pouring 150 mL of boiling water to one heaped teaspoon (3 g) of chamomile flowers. It is kept covered for 5–10 minutes and passed through a strainer (Bisset 1994). It has been found that the tea contains the spasm-reducing (spasmolytic) compounds—the flavonoids. The tea, however, cannot reduce internal inflammation because it has extremely low amounts of the anti-inflammatory compounds, which are mainly found in the essential oil. The tea contains only 1%–3% of the essential oil. However, if the tea is externally applied, it reduces inflammation (Schilcher 2005b).

1.5.1.2 Preparation of Tincture and Extract

To prepare tincture or extract, the dried chamomile flowers are homogenized at room temperature in ethanol–water and the liquid is evaporated. For tinctures, the ratio of ethanol to water is kept at 1:5 (Schilcher 2005b). The tincture can be taken in place of tea and is more effective (Bisset 1994). About 10–15 drops of tincture can be added to a glass of tepid water and used for gargle (Salamon 1993).

For extracts, the ratio of ethanol to water is kept at 1:1. The extracts are further dried and concentrated into viscous extracts and added to gels, ointments, and creams. Dry extracts are used to prepare tablets, capsules, and coated pills (Schilcher 2005b).

A high-quality extract should have one of the standard characteristics mentioned in Table 1.1.

1.5.1.3 Essential Oil

The essential oil of chamomile is present in the whole plant. However, the essential oil content is higher in the flowers than in other parts of the plant, and also has higher levels of useful compounds. Therefore, the essential oil of the flowers is mostly used for medicinal and aromatic purposes. The essential oil of chamomile is obtained by the

TABLE 1.1
Standard Characteristics of Chamomile Extract

S. No.	Ethanol–Water Extract (g)	Blue Essential Oil (mg)	(–)-α-Bisabolol (mg)	Chamazulene (mg)	Apigenin 7-Glucoside (mg)
1.	100	150–300	50	3	150–300
2.	100	170	50	—	10–40
3.	100	200	—	—	150

Source: Adapted from Schilcher, H., In R. Franke and H. Schilcher (eds.), *Chamomile: Industrial Profiles,* CRC Press, Boca Raton, FL, 2005b. With permission.

process of steam distillation or hydrodistillation, in which the flowers are subjected to high pressure, temperature, and steam to separate out the essential oil from them. The oil is deep blue or ink blue in color and has a characteristic sweet, grassy smell. It may turn green and then dark brown on oxidation and lose its therapeutic value (Shutes 2012). At the time of distillation, it is extremely concentrated. The quality of the essential oil may differ from one variety of chamomile plant to another, but the various pharmacopoeias clearly mention that to be used for medicinal purpose, the oil content should be 0.4% in the flowers. The oil is prone to vaporization and decomposition, and so it has to be stored carefully in dark bottles under the prescribed temperature.

Essential oils are absorbed into the body on inhalation and through the skin. The compounds penetrate the skin and enter the bloodstream and act as medicines. The essential oil of chamomile is extensively used in aromatherapy, massage, and baths.

1.5.1.3.1 Aromatherapy

Aromatherapy is a technique of healing where the patient is made to inhale the vapors of the essential oil. A few drops of chamomile oil are applied on a piece of cloth or handkerchief or tissue and slowly inhaled. Sometimes a few drops of oil are added to hot water and the steam is inhaled. Chamomile oil vapor is used extensively in aromatherapy to calm a person and reduce pain and anxiety (Ford-Martin and Odle 2005).

1.5.1.3.2 Massage

A massage with oil enables the medicinal compounds to penetrate the skin and enter the bloodstream. For the purposes of massages, the chamomile oil used is diluted with other oils such as olive oil, sunflower oil, or lavender oil. The oil is gently rubbed or massaged on to the inflicted part.

1.5.1.3.3 Bath

In many disease conditions, a hot bath or a cold bath is given to a patient. In hot baths, warm to hot water is used and in cold baths, cold water or ice is used. A few drops of chamomile essential oil are added for healing purposes. Sometimes whole chamomile flowers are put in a small bag and kept in the bath.

1.5.1.3.4 Compress

A compress is made by steeping a cloth or a towel in a bowl of hot (hot compress) or cold (cold compress) water. A few drops of chamomile oil are added in the water before steeping the cloth or towel. This compress is then applied to the affected part.

1.5.1.4 Disease Conditions in Which Chamomile Is Used

Chamomile is used in the traditional medicines in the treatment of several conditions such as appetite enhancement, asthma, bladder problems, bleeding, blood purifying, bronchitis, callouses, children's diseases, colds, colic, colitis, corns, cramps, dandruff, digestion problems, dizziness, drug withdrawal, earache, eye problems, gas, headache, hemorrhage, hemorrhoids, inflammation, insomnia, jaundice, kidney problems, menstrual problems, migraine, nervous disorders, pain, parasites, spleen disorders, swelling, toothache, worms, and wounds (Salamon 1993). The *Gale Encyclopedia of Alternative Medicine* (2005) lists about 50 disease conditions in humans where chamomile can be used. The homeopathic system (Iyer 1994) and the Unani system (Rashid and Ahmad 1994) also use chamomile to treat a variety of disease conditions. A list of the diseases and the effect of chamomile administration is compiled and provided in Table 1.2.

TABLE 1.2
Disease Conditions and Use of Chamomile

S. No.	Disease/Ailment	Effect of Chamomile
1.	Alcohol withdrawal	Calming and restorative, nerve tonifying
2.	Anorexia nervosa	Reduces anxiety and depression by stimulating appetite, relax the body. The essential oil is used, which is inhaled, massaged, or put in bath water
3.	Anxiety	Reduces phobias and panic disorder by promoting general relaxation of the nervous system. Chamomile acts as an adaptogen by promoting adaptability to stress
4.	Asthma	Promotes free breathing. Essential oil is inhaled to reduce obstruction in the airways
5.	Athlete's foot	Reduces symptoms. Essential oil is applied directly to the toes. The oil can be added to bath water as well
6.	ADHD	Calms the person. Chamomile extract is used for the treatment
7.	Binge eating disorder	Reduces stress, thereby reducing the disorder
8.	Boils	Fights infection. Chamomile is to be applied topically
9.	Bruxism	Prevents grinding of teeth. Chamomile acts as an antispasmodic and central nervous system relaxant. Chamomile is prescribed before going to bed
10.	Bunions	Relieves pain. Promotes wound healing. Used chamomile tea bag is applied to the bunion, which may prove helpful. Massaging with essential oil of chamomile or a cream containing chamomile may provide relief

(*Continued*)

TABLE 1.2 (*Continued*)
Disease Conditions and Use of Chamomile

S. No.	Disease/Ailment	Effect of Chamomile
11.	Burns	Reduces anxiety. Chamomile tea is recommended
12.	Canker sores	Existing sores are treated with tea. Compresses soaked in the tea are recommended to be applied directly to the mouth. The tea can also be swished around in the mouth for several minutes
13.	Chicken pox	Aids in sleep or promotes sleep
14.	Chills	Prevents chills and cold intolerance. Chamomile tea is recommended
15.	Colic	Reduces bowel inflammation and gas. Chamomile tea is recommended
16.	Conjunctivitis	Prevents discomfort of the eye. An eyewash is made of two to three teaspoons of chamomile flowers added to boiling water to make tea. The tea is cooled. A cool compress is made and put over the eye. Damp tea bags of chamomile may also be used
17.	Constipation	Stimulates movement of digestive and excretory systems
18.	Corns	Thickened skin is dissolved, providing relief. One teaspoon of lemon juice, one teaspoon of dried chamomile flowers, and one crushed garlic clove can be directly applied to dissolve thickened skin
19.	Cradle cap	Oil production of the skin is slowed down. Tannins in the chamomile tea can slow down this process. Chamomile tea can be rubbed onto the skin with a cloth several times per day
20.	Cuts and scratches	Repairs skin damage and encourages new cell growth. Chamomile oil can be sprayed onto the affected area
21.	Dermatitis	Provides relief. Chamomile ointment may be applied to the affected area
22.	Diarrhea	Provides relief. Chamomile infusion to be provided throughout the day
23.	Diverticulitis	Reduces inflammation in cases of uncomplicated diverticulitis
24.	Dry mouth	Stimulates salivary flow. Chamomile tea is recommended
25.	Eczema	Reduces inflammation. Chamomile ointment is used
26.	Epilepsy	Chamomile creates soothing mood. Essential oil is inhaled
27.	Fibromyalgia	Soothes muscle and joint pain. Chamomile tub soak (bath) or compress is recommended
28.	Fractures	Calming effect. Chamomile tea is recommended
29.	Fungal infections	Antifungal. Chamomile tea is used. The used tea bag can be put on the area of infection
30.	Gas	Relieves gas. Chamomile tea is recommended

TABLE 1.2 (*Continued*)
Disease Conditions and Use of Chamomile

S. No.	Disease/Ailment	Effect of Chamomile
31.	Gastritis	Counteracts free radicals and inhibits *Helicobacter pylori*. Chamomile tea is used
32.	Heartburn	Provides relief. Chamomile tea is used
33.	Holistic dentistry	Sedative effect and promotes relaxation. Tea or infusion is used
34.	Hypertension	Relieves stress. Essential oil is used
35.	Indigestion	Provides relief. Chamomile tea is used
36.	Inflammatory bowel disease	Reduces inflammation, reduces spasms, antibacterial action. Flowers of chamomile are soaked in water for 10–14 minutes and the tea is taken 3–4 times daily
37.	Insomnia	Promotes sleep. Chamomile tea is used. Putting chamomile flowers inside the pillow is also recommended
38.	Juvenile rheumatoid arthritis	Detoxification of body to reduce symptoms. Chamomile oil massage is recommended
39.	Knee pain	Reduces spasms and swellings. Chamomile tea and oil massage is recommended
40.	Low back pain	Reduces spasms. Chamomile tea and oil massage is recommended
41.	Measles	Reduces restlessness. Chamomile tea is used
42.	Ménière's disease	Promotes relaxation. Chamomile tea and chamomile oil massage is recommended
43.	Menstrual problems	Relieves mood swings, tension, and cramps. Chamomile tea is recommended. Essential oil massage is also recommended
44.	Nausea	Relieves symptoms of nausea and vomiting. Chamomile tea is used
45.	Osteoarthritis	Relieves symptoms. Massage with chamomile oil is recommended
46.	Ear (otitis media)	Reduces the congestion of upper respiratory tract infections
47.	Ovarian cysts	Stimulates blood circulation and healing in ovaries. Compress, made of towels soaked in chamomile oil, wrapped around a hot water bottle is applied to the lower abdomen
48.	Psoriasis	Relief of symptoms. Warm water bath with chamomile flowers is recommended
49.	Radiation injury	Reduces skin inflammation following radiation therapy. Chamomile cream is used
50.	Rashes	Relieves symptoms. Chamomile tea is recommended
51.	Rheumatic fever	Relieves pain. Massage with chamomile oil is recommended

(*Continued*)

TABLE 1.2 (*Continued*)
Disease Conditions and Use of Chamomile

S. No.	Disease/Ailment	Effect of Chamomile
52.	Rosacea	Soothes irritated skin. Cold compress of chamomile tea is recommended
53.	Scarlet fever	Promotes relaxation. Bath with tepid infusion of chamomile is recommended
54.	Stomach ache	Relieves upset stomach, gas, and stomach spasms. Chamomile tea is recommended
55.	Teething problems	Relieves pain. Cloth dampened with chamomile tea is placed in the freezer and used in place of a freezable toy

Source: Salamon, I., *The Modern Phytotherapist*, 13–16, 1993; Ford-Martin, P. and Odle, T. G. in Longe, J.L., ed., *Gale Encyclopedia of Alternative Medicine*, Second Edition, Volume I (A–C). Farmington Hills, MI: Thomson Gale, 2005, p. 123; Cooper, A. in Longe, J.L., ed., *Gale Encyclopedia of Alternative Medicine*, Second Edition, 2005, Encyclopedia.com. http://www.encyclopedia.com/doc/1G2-3435100699.html. Accessed March 8, 2014; Rowland, B. and Odle, T. in Longe, J.L., ed., *Gale Encyclopedia of Alternative Medicine*. 2005. Encyclopedia.com. http://www.encyclopedia.com/doc/1G2-3435100748.html. Accessed March 8, 2014; Turner, J. in J.L. Longe, ed., *Gale Encyclopedia of Alternative Medicine*. 2005. Encyclopedia.com. http://www.encyclopedia.com/doc/1G2-3435100768.html. Accessed March 8, 2014.

1.5.1.5 Herbal Formulations of Chamomile

There are several herbal medicinal formulations of chamomile available in the market in different countries. These are in the form of tablets, capsules, oils, creams, lotions, ointments, soaps, and shampoos. The U.S. Natural Medicine Comprehensive database lists 1154 products containing chamomile (Therapeutic Research Faculty 2012). In Germany, around 150 medicinal preparations are made from chamomile extracts in combination with other plant extracts and at least 18 preparations have the chamomile compounds as the sole ingredient (Schmidt and Vogel 1992). Chamomile drug is mostly sold all over the world with its generic name (Chamomile generic 2012) as well as branded products. There are some branded products as well and some well-known branded formulations of chamomile (World Standard Drug Database 2012). Some of these formulations are listed in Table 1.3.

1.5.1.6 Pharmacopoeias and Monographs

Chamomile is included in the pharmacopoeia of many countries, such as the European, British, French, German, and others (Schilcher 2005a). In addition to the pharmacopoeia, chamomile is also mentioned in the monographs of the German Commission E, European Scientific Cooperative on Phytotherapy (ESCOP), and World Health Organization (WHO).

1.5.1.6.1 European Pharmacopoeia

The *European Pharmacopoeia* is extensively used all over the world as an authoritative reference for manufacturing quality chamomile drug. It provides a description

TABLE 1.3
List of Some Branded Chamomile Formulations

S. No.	Name of the Formulation	Brand	Website
1.	Chamomile ointment	Kamillosan	http://www.medapharma.de/otc/kamillosan/
2.	Carminative tea	Djehuty	http://www.cherryfones.com/carminative-tea.html
3.	Massage balm	Weleda	http://www.weleda.co.uk/aches-+amp-pains/massage-balm-with-calendula-50ml/invt/204004/
4.	Chamomile liquid	HealthAid	http://www.healthaid.co.uk/shopexd.aspx?id = 381
5.	Herbal tea	Jan de Vries	http://www.jandevrieshealth.co.uk/store_main.asp?int_catalog_id = 1&int_category_id = 12&int_subcategory_id = 0&prod = 140
6.	Chamomile flower capsules	Bio-health	http://www.baldwins.co.uk/herbs/capsules/bio-health-chamomile-flowers-250mg-60-vegetarian-capsules
7.	St John's Wort herbal complex	Vega nutritionals	http://www.vegavitamins.co.uk/st-john-s-wort-herbal-complex-prd-256.html
8.	Daily gum and toothpaste	Corsodyl	http://www.corsodyl.co.uk/maintenance/toothpaste.shtml
9.	Sinose spray	Salcura	https://www.salcuraskincare.com/product/sinose/
10.	Elena's trinity soap and shampoo	Elena's Nature Collection	http://elenasnaturecollection.co.uk/our-skin-care-products/#ecwid:category = 1923096&mode = product&product = 8734354

of the morphological and cellular characteristics of the chamomile flowers to enable easy identification using microscopy. It also provides the guidelines to identify the essential oil, methods to detect any adulteration, and guidelines for proper storage, and labeling to ensure the safety of the finished products. An excerpt from the pharmacopoeias is provided below (Schilcher 2005a).

1. Description
   a. Morphological characteristics
      i. Bracts: Involucres in one to three rows, ovate to lanceolate, brownish gray, scarious margin
      ii. Receptacle: Elongated, conical, hollow, without pale
      iii. Ligulate florets: Twelve to ten, white, marginal, elongated ligule, corolla has brownish yellow tube at base
      iv. Tubular florets: Several dozen, yellow, five-toothed corolla tube
      v. Androecium: Five stamens, syngenecious, epipetalous
      vi. Gynoecium: Same in ligulate and tubular florets; ovary inferior, ovoid to spherical; style long; stigma bifid

   b. Cellular characteristics
      i. Bracts: Cells thin walled, elongated sclereids in the central region, stomata
      ii. Ligulate florets: Epidermis has thin-walled, polygonal, slightly papillose cells; outer epidermis has sinuous and striated cells
      iii. Tubular florets: Epidermis has longitudinal elongated cells, small groups of papillae present near apex of lobes
      iv. Glandular trichomes: Present on the outer surface of the bract of the corollas of both ligulate and tubular florets, short stalk and head on 2–3 tiers of cells
      v. Androecium: Anther lobes contain calcium oxalate crystals; pollen 30 µm, spherical to triangular with three pores, spiny exine
      vi. Gynoecium: Sclerous ring at the base of the ovary, ovary wall has longitudinally elongated cells with numerous glandular trichomes, alternating with fusiform, radially elongated cells containing mucilage, inner tissues containing calcium oxalate crystals; stigma cells form rounded papilla
2. Essential oil
   a. Essential oil and extract: 4 mL/kg in dried flowers, clear intensely blue viscous liquid, intense, characteristic odor, apigenin-7-glucoside (0.25%), azulenes, levomenol, bornyl acetate, en-yn-dicycloether. Detected by thin layer chromatography (TLC) and gas chromatography–mass spectrometry (GCMS)
3. Storage
   a. The container should be well filled and airtight. The container should be protected from light and stored at a temperature not exceeding 26°C.
4. Labeling
   a. The type of oil should be indicated in the label, such as "rich in bisabolol oxides" or "rich in levomenol."

1.5.1.6.2 German Commission E Monograph

The German Commission E monograph provides the botanical name of the chamomile plant. No detailed botanical description of the flowers is provided. It specifies the essential oil content in the flowers used in medicines. It also provides guidelines for the therapeutic uses, dosage, and the mode of administration (Carle and Gomma 1991/92; Schilcher 2005a).

1. Description of the drug
   a. Fresh or dried heads of *M. recutita* L. (synonym: Chamomilla recutita (L.) Rauschert) and their preparation of effective doses.
2. Essential oil
   a. Essential oil and extracts: The flowers should contain not less than 0.4% (v/w) of volatile oil. The main constituents are (–)-α-bisabolol or bisabolol oxides A and B, matricarin, apigenin, and apigenin-7-glucoside

3. Therapeutic uses
   a. External Uses: Inflammation of skin and mucous membrane, bacterial diseases of skin, oral cavity and gums, respiratory tract (inhalation of vapors), inflammation of the anogenital region
   b. Internal Uses: Spasms and inflammation of the gastrointestinal region
4. Contraindications
   a. Not known
5. Dosage
   a. For adults
      i. Tea: Boil 3 g of chamomile flowers in 150 mL water. Keep it covered for 5 –10 minutes. Strain with a tea strainer. For gastrointestinal disorders drink three to four times a day between meals. Use as a gargle in case of inflammation of mucous membranes of the mouth or throat
      ii. Poultices: 3%–10% of infusions
      iii. Bath: 50 g of flower in 10 L
      iv. Semisolid preparation: 3%–10% of the preparation should contain chamomile
6. Mode of administration
   a. Liquid and solid preparation for external and internal application

1.5.1.6.3 European Scientific Cooperative on Phytotherapy Monograph

The *ESCOP Monograph* essentially provides the same guidelines as the *European Pharmacopoeia* as far as chamomile is concerned. In addition, it specifies the quality of the essential oil and extract, the therapeutic uses, doses, methods of administration, and contraindications (Schilcher 2005a).

1. Description
   a. Complies with *European Pharmacopoeia*
2. Essential oil
   a. Essential oil and extract
      i. Should contain no less than 4 mg/kg of blue essential oil (0.5%–1.5%)
      ii. Apigenin-7-glucoside (0.5%)
      iii. Sesquiterpenes (bisabolol A, bisabolol oxides A and B, bisabolone oxide A) (50%)
      iv. *cis*- and *trans*-en-yn-dicycloethers (25%)
      v. Matricin (converted to chamazulene) (15%)
      vi. Coumarins (herniarin and umbelliferone), phenolic acids, and polysaccharides (up to 10%)
3. Therapeutic uses
   a. Internal Uses: Gastrointestinal spasms, flatulence
      b. External Uses: Minor inflammations and initiations of skin and mucosa of oral cavity and respiratory tract (inhalation of vapors), and anal and genital region (bath and ointments)

4. Dosage
   a. Internal Use
      i. For adults
         A. Tea: 3 g of the drug is added to 150 mL of hot water, 3–4 times a day
         B. Fluid extract: One part drug to two parts solvent (50% ethanol preferred), 3–6 mL daily
         C. Dry extract: 5–300 mg three times daily
      ii. For elderly: Same as adults
      iii. For children: Proportion of adult dose according to age or body weight
   b. External Use
      i. Compress: 3–10 m/v of infusion, 1% v/v fluid extract, or 5% v/v tincture
      ii. Rinses, Gargle, and Bath: 5 g drug or 0.8 g of extract per liter of water
      iii. Solid/Semisolid Preparation: 3%–10% m/v of extract in the preparation
      iv. Vapor: 10–20 mL alcoholic extract per liter of hot water
5. Method of administration
   a. Oral, local application, and inhalation
   b. No restriction on duration
6. Contraindications
   a. Sensitivity to *Matricaria* or other *Compositae*

1.5.1.6.4 WHO Monograph

The WHO monograph provides a list of common names of chamomile, and botanical and microscopic description of the flowers. It also provides specifications for the essential oil and the purity tests such as those for microbes, pesticide residues, and heavy metals in the drug. It indicates the uses of the drug supported by clinical data (WHO 1999).

1. Definition
   a. The drug is the dry flowering heads of *C. recutita* (L.) Rauschert (synonyms: *M. chamomilla*, *M. recutita* L., *M. suaveolens*). The monograph also provides selected vernacular names such as Babuna, German chamomile, Chamomile, Kamille, and Manzanilla
2. Description of flower heads
   a. Morphological characteristics
      i. Peduncle: Short, up to 2.5 cm long, weak brown to dusky greenish yellow, longitudinally furrowed, more or less twisted
      ii. Receptacle: Conical, narrow, hollow
      iii. Involucre: 20–30 imbricate, oblanceolate and pubescent scales
      iv. Ligulate florets: A few, white, pistillate, three-toothed, four-veined
      v. Tubular florets: Numerous, yellowish orange to pale yellow, perfect, without pappus
      vi. Achenes: Obovoid, faintly, three to five ribbed, no pappus, slightly membranous crown
   b. Cellular characteristics
      i. Receptacles
      ii. Bracteoles: Schizogenous secretory ducts present; phloem fibers present; vessels spiral, annular, reticulate, pitted

   iii. Androecium: Pollen spherical or triangular, numerous spines
   iv. Gynoecium: Ovaries do not have lignified scale at the base; ovary walls have longitudinal bands of small mucilaginous cells; stigma has elongated papilla at the apex
   v. Glandular hairs: All parts bear glandular hairs with short biseriate stalk and elongated head, several tiered, and each made of two cells
3. Essential Oil
   a. Blue color, not less than 0.4% v/w of essential oil. Total volatile oil is to be determined. For volatile oil, TLC and GLC are to be used. For detection of flavonoids, high-performance liquid chromatography is to be used.

1.5.1.6.5 Compendium of Monographs, Canada

The compendium of monographs of Canada has been developed by Natural Health Products Directorate (NHPD) in 2009 and contains a monograph on chamomile. The monograph provides different names of chamomile and specifies administration, dosage, and risk information. It specifies that the formulations should be made according to the *British Pharmacopoeia*, *European Pharmacopoeia*, and *United States Pharmacopeia* (Health Canada 2009).

1. Proper names
   a. *M chamomilla* L. (Asteraceae) (synonyms: *M. recutita* L.; *C. recutita* L. Rauschert)
2. Common names
   a. German chamomile, Chamomile
3. Source material
   a. Flower
4. Route(s) of administration
   a. Oral, Topical, Buccal (rinse or gargle)
5. Dosage
   a. Oral: Children (2–4 years) and adolescents (5–9 years) should be given 0.3–0.6 g dried flowers per day, and adolescents (10–14 years) and adults (≥14 years) 0.8–24 g dried flowers per day
   b. Topical and buccal: Preparations containing the equivalent of 3%–10% dried flower; 1% v/v fluid extract, 5% v/v tincture
6. Risk information
   a. Caution(s) and warning(s): Consult a health-care practitioner if symptoms persist or worsen
   b. Known adverse reaction(s): Hypersensitivity, such as allergy, has been known to occur in which case, discontinue use
7. Specifications
   a. The finished product must comply with the minimum specifications outlined in the current NHPD Compendium of Monographs. The medicinal ingredient may comply with the specifications outlined in the pharmacopoeial monographs, the *British Pharmacopoeia*, *European Pharmacopoeia*, and *United States Pharmacopeia*.

1.5.1.7 Quality, Safety, and Efficacy Issues of Chamomile Herbal Formulations

The basic raw material of chamomile drugs is the plant, which is mostly cultivated. The issue of quality begins at the cultivation stage. The drugs may be contaminated with pesticides, heavy metals, harmful microbes, and radioactive materials (Salamon and Plačková 2007; Alwakeel 2008). More often than not the drugs and essential oil are found to be adulterated (Martins et al. 2001; Nascimento et al. 2005). Often the packaging is unhygienic, which encourages microbial growth. These issues of quality, safety, and efficacy are described briefly in Sections 1.5.1.7.1 through 1.5.1.7.10.

1.5.1.7.1 Adulteration of Flowers

Chamomile formulations available in the market have been occasionally found to be adulterated with the flowers of other species such as *A. arvensis*, *A. cotula*, *A. montana*, *A. tinctoria*, *C. suaveolens*, *Chrysanthemum leucanthemum*, *M. perforata* (Mann and Staba 1986), *A. nobilis* (Uzma and Khan 1998), *M. aurea*, and *Inula vestita* (Ahmad et al. 2009). Considering the enormous levels of adulteration, the correct botanical identification of the drug assumes great importance. The drug in its powdered form can be microscopically and analytically examined and matched with the description of the drugs as provided in the various pharmacopoeias. Several macroscopic, microscopic, and analytical examination of the powdered chamomile drug have been carried out and further detailed descriptions have been provided (Rashid and Ahmad 1994; Uzma and Khan 1998) to detect adulterations.

1.5.1.7.2 Adulteration of the Essential Oil

The essential oil has been found to be adulterated with the essential oil of the tree *Vanillosmopsis erythropappa*. The oil from this tree is rich in (−)-α-bisabolol and is cheaper than chamomile oil (Leung 1980). Researchers have found that the oil of *M. matricarioides* is also chemically similar to chamomile (Loomis et al. 2004). However, the isotope ratio mass spectrometry (IRMS) study on the oil of *V. erythropappa* shows that the oil has a different chemical composition than chamomile oil. These findings help in detecting and checking adulteration (Verpoorte et al. 2005).

1.5.1.7.3 Pesticide Residues

Chamomile drug samples have been found to contain pesticide residues, which could pose as a health hazard, such as endocrine disruption or even cancer. A study in Egypt found that the chamomile samples contained the pesticide chlorpyrifos at 0.01 mg/kg (Farag et al. 2011). The limit of chlorpyrifos has been set at 0.2 mg/kg by the *European Pharmacopoeia*. The limits have been set at 5.0 mg/kg for seeds, 1.0 mg/kg for fruits, and 1.0 mg/kg for roots by the Codex Alimentarius Commission of WHO (Kosalec et al. 2009). High levels of chlorpyrifos could cause neurological damage and attention deficit hyperactivity disorder (ADHD) in infants (Rauh et al. 2006). A study by Lozano et al. (2012) found that a large number of chamomile teas sold in the European Union contained banned pesticides and also pesticide levels beyond the prescribed limit.

1.5.1.7.4 Heavy Metals

High levels of heavy metals, such as cadmium and lead, are harmful to humans in many ways. These cause a variety of ailments, and are toxic and carcinogenic to humans. Heavy metals have been detected on chamomile samples in a study (Alwakeel 2008). The study found that the chamomile samples contained lead, 0.13 ppm; mercury, 0.08 ppm; aluminum, 1.7 ppm; cadmium, 0.6 ppm; copper, 0.3 ppm; iron, 0.6 ppm; zinc, 943 ppm; and potassium, 228 ppm. It is to be noted that the permissible limits of heavy metals in herbal drugs are lead, 2.0 ppm; mercury, 0.5 ppm; aluminum, 0.2 ppm; cadmium, 0.2 ppm; iron, 15 ppm; and zinc, 5 ppm. The levels of the heavy metals were not alarming, but the levels of aluminum were much higher than the permissible limits. Aluminum is known to cause Alzheimer's disease (Alwakeel 2008). Testing for heavy materials is therefore important for maintaining the quality of the drug.

1.5.1.7.5 Microbial Contamination

Chamomile drug samples have been found to be contaminated with microbes, some of which cause severe diseases and some of these are potentially fatal. Many microbes produce mycotoxins that are teratogenic and carcinogenic. The microbes identified in chamomile samples are *Bacillus cereus*, *Clostridium perfringens*, *Salmonella*, *Escherichia coli*, *Fusarium* spp., *Penicillium* spp., *Absidia* spp., *Cladosporium* spp., *Paecilomyces* spp., *Cryptococcus albidus*, *C. laurentii*, *Rhodotorula glutinis*, *R. mucilaginosa*, *Aspergillus* spp., yeast, mold, *Rhizopus* spp., *Ulocladium* spp., *and Mycelia sterilia* (Mimica-Dukic et al. 1993; Martins et al. 2001; Foote 2002; Carvalho et al. 2009). A study on decontamination methods of microbes advocated stringent measures to guarantee the quality and safety of chamomile drugs (Maximino et al. 2011).

1.5.1.7.6 Other Impurities

The other impurities include foreign matters such as insects, animal matter, and sand. In several studies, it was found that commercial chamomile samples contained significant amounts of foreign matter (Nascimento et al. 2005; Falkowski et al. 2009). Insects such as *Lasioderma serricorne* were found in the drug (Pons et al. 2010). Such contaminants are, needless to say, undesirable in the drug.

1.5.1.7.7 Packaging

The tea bags and containers that hold the drug are important. This is because the hygiene, and the physical and chemical stability of the drug depend on the packaging. A study has recommended the use of CO_2 as an alternative to fumigation with synthetic chemicals for insect control in containers during shipment (Pons et al. 2010). The container of the drug, such as the tea bags or bottles, should be sterilized so that the shelf life of the drug is improved. The stability of the contents should be checked through TLC, GCMS, and so on, which help in detecting the presence or absence of the relevant compounds.

1.5.1.7.8 Labeling

Labeling is to ensure that the quality of information given to the consumer is good (Kunle et al. 2012). The label of the drug container should contain the relevant information about the origin, quality, safety, and dosage of the drug. The label should contain the warnings or risk factors of the drug.

1.5.1.7.9 Safety

The toxicity studies of the chamomile drug are important to ensure that it does not prove harmful or fatal and is safe for use. Several toxicity studies have been carried out with the chamomile drug. Chamomile drug has tolerable effects (Roder 1982) and there appear to be no reports of any gross toxicity and allergenicity caused either by the crude preparations or by the individual compounds of chamomile (Habersang et al. 1979). For testing the toxicity, physicians recommend a patch test on the skin. The label of the container of the chamomile drug should carry a warning about the toxicity effects.

1.5.1.7.10 Efficacy

The efficacy of the drug is to be indicated on the label of the container. To establish the efficacy of the chamomile drug, several pharmacological studies have been carried out on humans, animal models, microbes, and so on. The individual constituents or the compounds of the flower extractable in the essential oil or through the use of solvents determine the specific activities of the drug. The activities of the compounds have been identified on the basis of their effect on the experimental models. The tests have revealed that chamazulene possesses antioxidant and anti-inflammatory properties and provides protection against liver damage. Bisabolol protects against ulcers. Apigenin has anti-inflammatory and spasmolytic properties. The polysaccharides are immunostimulating.

1.5.1.8 Methods to Ensure Quality, Safety, and Efficacy of Chamomile Drugs

Several methods are employed to assess and ensure the quality, safety, and efficacy of chamomile drugs. The quality issues mentioned previously, such as adulterants, pesticides, heavy metals, microbes, and other material, can be easily detected macroscopically, microscopically, and through various analytical tools such as scanning electron microscopy, TLC, GCMS, ultraviolet spectrophotometry, IRMS, and microbial culture methods. Many chemical tests are also carried out to detect the traces of pesticides and heavy metals. Some of the methods are described in Sections 1.5.1.8.1 through 1.5.1.8.6 (WHO 1998, 2011).

1.5.1.8.1 Detection of Adulterants of Chamomile Flowers

The chamomile drug comprising dry flowers can be subject to macroscopic and microscopic observation and compared to the description of the actual drug available in the literature. The macroscopic examination includes visual examination of the drug, which determines the size of the chamomile flowers, the color of flowers, and odor and taste. Chamomile flowers possess a characteristic odor and can be identified by its organoleptic properties.

Several pharmacopoeias and research papers have provided a detailed description of the features of the drug observed under the microscope. These are listed under Section 1.5.1.6.

1.5.1.8.2 Detection of Adulteration of the Essential Oil

The authenticity of the essential oil of chamomile can be described by its visual appearance, odor, the specific compounds in it, and also the specific percentage of those compounds of the oil that it possesses. The chamomile essential oil is known to contain chamazulene, (–)-α-bisabolol, bisabolol oxides A and B, bisabolone oxide A, and farnesene, among others. A complete list of the chemical compounds is available in the literature and is also provided in Chapter 4. For testing the oil, the flowers are subjected to steam distillation. The distilled oil is collected and studied for its properties such as color and odor, and then tested through the methods of TLC and GCMS.

1.5.1.8.3 Detection of Total Volatile Oil Content

The chamomile oil is volatile, which means it has the ability to vaporize at room temperature. One of the methods to determine the suitability of the chamomile drug is the amount of essential oil or volatile oil content in it. To determine the total volatile component in the chamomile flowers, the flowers are steam distilled in a Clevenger-type apparatus. The volume of the oil distilled per 100 g flowers is expressed in percentage. This percentage indicates the total volatile oil content.

1.5.1.8.4 Detection of Pesticide Residues

The pesticide residues are found in chamomile drug due to agricultural practices during cultivation. The pesticide residues usually have compounds such as chlorinated hydrocarbons or sulfur-containing dithiocarbamate or organophosphorus. These can be detected by column chromatography (CC) and GC. A purified chamomile extract is specifically prepared for the detection of the pesticide residues in it by GC.

Abdel-Gawad et al. (2011) suggested that the insecticide ^{14}C-ethion could be satisfactorily eliminated from the essential oil of chamomile if adsorbents such as calcium oxide and sawdust were added during the distillation process. Such methods that could efficiently eliminate pesticide residues need to be developed.

1.5.1.8.5 Detection of Heavy Metals

For detecting the levels of heavy metals such as lead and cadmium, several methods of analysis are available to choose from, such as inverse voltammetry or atomic absorption spectrometry.

1.5.1.8.6 Detection of Microorganisms

To detect the microorganisms present in chamomile, a sample of the drug is cultured in a liquid broth or semisolid culture medium in agar. Within a day or 2, the microorganisms grow in the broth or agar medium. These are identified according to their growth or no growth in a specific medium, the type of colony formation, or their morphology.

1.5.1.9 Good Manufacturing Practices for Herbal Formulations per World Health Organization Guidelines

The guidelines for Good Manufacturing Practices (GMP) have been developed by the WHO for herbal medicines. These guidelines are meant to be adopted by the member countries to ensure the quality, safety, and efficacy of the herbal medicines made in their own countries (WHO 2007). The GMP guidelines describe the complete process of manufacture of the herbal formulation right from the collection or harvesting of the plant to the packaging and marketing of the finished product. The guidelines also specify the infrastructural, sanitary, equipment, and management standards that need to be followed by the manufacturers.

1.5.1.9.1 Quality Assurance in the Manufacture of Herbal Medicines

Quality assurance includes all those matters that influence the quality of the herbal drug. Quality of the herbal drugs can be assured through analytical techniques such as high-performance thin-layer chromatography, GC, atomic absorption, and capillary electrophoresis. The WHO guidelines also specify that the manufacturer must assume responsibility for the quality of the drug or formulation.

1.5.1.9.2 Good Manufacturing Practice for Herbal Medicines

All manufacturing practices should be clearly defined and reviewed for consistency of the process. Operators who manufacture the drugs should be properly trained. Any complaints about the marketed drug should be attended to.

1.5.1.9.3 Sanitation and Hygiene

At all levels of manufacturing process, sanitation and hygiene should be practiced. This includes the sanitation and hygiene of the premises and the personnel employed.

1.5.1.9.4 Qualification and Validation

The infrastructure, premises, all equipment, processes and tests, and the documentation used for manufacture should be qualified and validated.

1.5.1.9.5 Complaints

A complaint in the manufactured drug should be reviewed and action should be taken. If necessary, the product should be recalled.

1.5.1.9.6 Product Recalls

A process should be enforced and person should be authorized to recall the defective products from the market. The process should be monitored and the recalled products should be stored in a place separate from the site of manufacture.

1.5.1.9.7 Contract Production and Analysis

Contracts given out to manufacture drugs should be correctly defined and controlled. All manufacturing and marketing processes should be as per the regulations and GMP.

1.5.1.9.8 Self-Inspection

The manufacturer should set up a self-inspection system and a team to inspect the quality aspects from time to time. The inspection item list should include the premises, personnel, equipment, validation of the processes and documents, and audit.

1.5.1.9.9 Personnel

The number of personnel should be adequate, trained, and aware of the GMP. Their job responsibilities should be well defined.

1.5.1.9.10 Training

The manufacture should provide training to the personnel in the GMP through approved training programs. In addition, the new recruits should be trained in the jobs they are responsible for.

1.5.1.9.11 Personal Hygiene

All employees should undergo health examinations and trained in the practices of personal hygiene. Direct contact should be avoided between the personnel and the raw materials, or the intermediate product or the finished product.

1.5.1.9.12 Premises

The premises should be located in an area that minimizes contamination. The premises should be constructed well to provide adequate light and ventilation, maintained well, cleaned, and disinfected.

1.5.1.9.13 Equipment

The equipment should be installed properly to avoid any kind of contamination. These should be calibrated from time to time. Cleaning should be done as per validated process.

1.5.1.9.14 Materials

All the materials used in the manufacturing process, such as the raw materials, chemicals, and packaging materials, should be suitable, tested for contamination, and stored carefully.

1.5.1.9.15 Documentation

The documents used for the manufacture and marketing of drugs, such as reference materials, should be authentic and properly recorded. The information on the label and packaging should be based on the correct documentation.

1.5.1.10 National Regulations for Herbal Formulations

Several countries have laws in place to regulate the manufacture and marketing of herbal medicines. A study by the WHO in 2005 revealed that 53 countries had regulations related to the traditional medicine (WHO 2005). Table 1.4 lists some of the countries that have legally binding national regulations in place, which also recommend the use of pharmacopoeia and monographs.

TABLE 1.4
List of Some Countries with National Regulations on the Use of Chamomile Drugs

S. No.	Country	Legally Binding Regulations
1.	Argentina	Resolution 144/98, Farmacopea nacional Argentina, United States Pharmacopoeia, European Pharmacopoeia, British Pharmacopoeia, European Scientific Cooperative on Phytotherapy (ESCOP) Monographs, and the WHO Monographs. Good manufacturing practices (GMP)
2.	Australia	The Therapeutic Goods Act, 1989, British Pharmacopoeia
3.	Brazil	RDC 48/2004, Farmacopéia Brasileira, GMP
4.	Canada	The Food and Drugs Act, 2003, Compendium of pharmaceuticals and specialties, Canadian drug reference for health professionals, Compendium of Nonprescription Products, United States Pharmacopoeia, Herbal medicines, Expanded Commission E Monographs, ESCOP Monographs, WHO Monographs, Pharmacopoeia of the People's Republic of China, Physicians' Desk Reference for Herbal Medicines, British Herbal Compendium, and British Herbal Pharmacopoeia, GMP
5.	Colombia	Decree 677 of 1995 and Decree 337 of 1998, United States Pharmacopoeia, Codex francés, and British Herbal Pharmacopoeia, GMP
6.	Croatia	GMP
7.	Egypt	Pharmacy Law no. 127 of 1955, Egyptian Pharmacopoeia, GMP
8.	Germany	The German Drug Law of 1976, Deutsches Arzneibuch (German pharmacopoeia, DAB), and the European Pharmacopoeia, GMP
9.	Hungary	"Healing products or paramedicine" 1987, Hungarian Pharmacopoeia, GMP
10.	India	The Drugs and Cosmetics Act, 1940, Unani Pharmacopoeia of India, GMP
11.	Israel	No national regulation, British Pharmacopoeia, French Pharmacopoeia, and United States Pharmacopoeia, GMP
12.	Iran	Regulation in 1996, British Pharmacopoeia (not legally binding), Pharmacopoeia of the People's Republic of China (not legally binding), National formulary of Iran (not legally binding), GMP
13.	Kenya	No national regulation, no monographs
14.	Pakistan	The Drugs Act of 1962, Tibbi Pharmacopoeia (not legally binding), GMP
15.	Poland	GMP
16.	Serbia	Law on use of herbal medication of 1993, European Pharmacopoeia, GMP
17.	Slovakia	Law of 1997, Pharmacopoeia Slovaca, Codex Pharmaceutical Slovacus, GMP
18.	Tasmania	GMP

TABLE 1.4 (*Continued*)
List of Some Countries with National Regulations on the Use of Chamomile Drugs

S. No.	Country	Legally Binding Regulations
19.	United Kingdom	Medicines Act, 1968 (2001/83/EC also applies), British Pharmacopoeia, GMP
20.	United States	GMP

Source: WHO, *National Policy on Traditional Medicine and Regulation of Herbal Medicines: Report of a WHO Global Survey,* World Health Organization, Geneva, 2005.

1.5.2 Homeopathy

Homeopathy is a system of therapy, which is based on symptom similarity. It works on the combined principles of two laws: (1) a group of symptoms present in a disease and (2) a group of symptoms caused by the effect of a drug on a healthy human. It means that if a drug in its crude form causes the symptoms of a particular disease in a healthy human, that drug in a heavily diluted form is used to treat the same symptoms in a diseased person. Samuel Christian Hahnemann, the founder of homeopathy, expressed it as *Similia similbus curenteur*, meaning "let likes be cured by likes" (Iyer 1994; WHO 2009; Homeopathy-Chamomilla 2012).

The *Materia Medica* used in homeopathic practice emphasizes that the name of the disease is not the leading feature, but the general character and nature of the disease combined with the constitutional peculiarities of the patient, and the general characteristics of the remedy are important for treatment. The general characteristics of chamomile, as described in the Homeopathic Materia Medica, are as follows (Iyer 1994).

The chief guiding symptoms belong to the mental and emotional group, which lead to this remedy in many forms of disease, especially in diseases of children, where peevishness, restlessness, and colic give the needful indications. Chamomilla is sensitive, irritable, thirsty, hot, and numb. Oversensitiveness from abuse of coffee and narcotics. Pains unendurable, associated with numbness. Night sweats. Child fretful, wants to be carried, wants things, and then does not want them, snappish. One cheek red and the other pale. Diarrhea and colic. Green stools, like rotten eggs, during period of dentition. Sleeplessness of children. Rheumatic pains that drive patient from bed. Excessive restlessness and tossing. Hot and thirsty. Wind colic. Skin moist and hot. Worse by heat, anger, during evening, before midnight, open air, in the wind, eructations. Better in children from being carried, warm, wet weather.

Complimentary: Follows Belladonna in diseases of children and useful in cases spoiled by the use of opium or morphine in complaints of children; Mag C.

1. Antidotes of Chamomilla: Camphor, *Pulsatilla*, nux vomica
2. Compare: Belladonna, *Bryonia*, coffee, *Pulsatilla*, sulfur

1.5.2.1 Disease Conditions

Chamomile is recommended in several disease conditions of the different body parts, such as those of the head and brain, eyes, ears, throat, teeth, and stomach. It is also used to treat pregnancy-related ailments. Specific conditions of women and infants are also treated using chamomile. Table 1.5 lists some of the disease conditions and the use of chamomile in homeopathy.

TABLE 1.5
Use of Chamomile in Some Disease Conditions in Homeopathy

S. No.	Category	Disease Conditions
1.	Head and brain	Rheumatic headache accompanied by tearing pains on one side of the head and earache
2.	Head and brain	Nervous headache caused by cold and sore throat
3.	Head and brain	Hysteria
4.	Head and brain	Epilepsy with headache before and after the spasm, and spasms of the facial muscles
5.	Eyes	Sore eyes of young infants. If eyes are glued together in the morning, chamomile solution in warm water may be applied
6.	Ears	Earache due to inflammation due to cold
7.	Ears	Hardness of hearing connected to cold and sore throat
8.	Throat	Bronchitis in the first inflammatory stage, especially for children
9.	Throat	Sore throat due to cold. Useful especially for children
10.	Teeth	Toothache in children and females, especially when the person has earache, faceache, before menstruation, or the person is of nervous or hysterical nature
11.	Stomach and abdomen	Sour stomach in nursing infants
12.	Stomach and abdomen	Colic or gripping pain in bowels. Chamomile is especially suitable for women and children. It is recommended for colic and pain in pregnant women
13.	Stomach and abdomen	Dyspepsia or indigestion. Effective where gastric derangements are brought about by fits of passion, sour eructations, and regurgitation of food
14.	Stomach and abdomen	Diarrhea, especially for infants. Recommended for condition of diarrhea after a cold
15.	Stomach and abdomen	Mild cases of jaundice, especially if the disease is caused by fits of passion. Useful for infants and it is recommended that one dose of one or two drops of the solution every 4 hours should be given
16.	Stomach and abdomen	Rheumatic fevers accompanied by tearing pains in body parts with a sensation of numbness in the parts
17.	Stomach and abdomen	Gastric and bilious fever accompanied by diarrhea or frequent stools, colicky pains, sleeplessness, or excitement
18.	Diseases of women	Menorrhagia with profuse pains in the abdomen and back

TABLE 1.5 (*Continued*)
Use of Chamomile in Some Disease Conditions in Homeopathy

S. No.	Category	Disease Conditions
19.	Diseases of women	Dysmenorrhea with pains like labor pains, violent abdominal cramps. Dark discharges of coagulated clots
20.	Pregnancy	Diarrhea during pregnancy
21.	Pregnancy	Hysterical fits or fainting during pregnancy, due to fits of anger or excitement
22.	Pregnancy	Palpitation of heart during pregnancy for nervous persons
23.	Pregnancy	Toothache during pregnancy in carious teeth and violent pains in teeth
24.	Pregnancy	Neuralgia during pregnancy and increased irritability
25.	Pregnancy	Miscarriage with excessive restlessness, severe pain in the back, pains resembling labor pains and each pain followed by discharge of dark colored blood
26.	Pregnancy	During labor pains if there is great mental excitement
27.	After childbirth	After delivery if there is lot of nervousness, restlessness, and excitement
28.	After childbirth	Lochia or discharges after childbirth. Chamomile is recommended if lochia is suppressed due to cold followed by diarrhea and colic
29.	After childbirth	Milk fever with nervous excitement, tenderness of the breasts
30.	Infants	Snuffles or obstruction of the nose in infants accompanied by runny nose
31.	Infants	Crying of infants if there is reason to think that it is crying due to some pain
32.	Infants	Colic in infants
33.	Infants	Restlessness and wakefulness in infants accompanied by flatulence and feverishness
34.	Infants	Teething (dentition)
35.	Infants	Prickly heat with fever and restlessness
36.	Infants	Discharge from ears with pain
37.	Infants	Rickets with restlessness and irritability, colic and diarrhea
38.	General	Sciatica when pains are worse at night
39.	General	Sleeplessness in children due to severe pain and in nervous women
40.	General	Toothache immediately on drinking coffee

Source: Iyer, T.S., *Beginners Guide to Homeopathy*, B. Jain Publishers, New Delhi, 1994.

1.5.2.2 Formulations in Homeopathy

Chamomile is used in the liquid form as a tincture in homeopathy. This tincture may be used by adding to water or to tiny sugar pellets. The process of making tincture is described in this section.

The whole plant of chamomile is used to prepare the tincture. The plant is harvested when it is at the flowering stage. This stage is considered to have optimum healing properties. The whole plant is cut into small pieces and macerated with equal parts of 35% alcohol and left for some time. This is followed by filtration to obtain a liquid. The liquid is in a very crude form and is called the mother tincture. The mother tincture is diluted repeatedly and used for therapy (Homeopathy-chamomilla 2012). It is believed that the higher the dilutions, the greater the effectiveness of the drug or potency. To make the dilutions, one part of mother tincture is taken and diluted with 99 parts of distilled water. It is shaken vigorously and the process is called *succussion*. This dilution is called 1c and is considered weak. To make stronger potencies, one part of 1c is mixed with 99 parts of distilled water to make 2c. Further dilutions repeated four times yield 6c, which is administered. Other potencies used are 30c and 200c (Olsen 2012).

1.5.2.3 Homeopathic Pharmacopoeia

The practitioners of homeopathic system of medicine follow *The United States Homeopathic Pharmacopoeia* and the *British Homeopathic Pharmacopoeia*, in addition to the *Homeopathic Materia Medica*.

1.5.2.3.1 The United States Homeopathic Pharmacopoeia

The Homeopathic Pharmacopoeia of the United States (HPUS) was published in 1878 and provides a description of the chamomile plant, the active principle, and the plant part used. It provides specification for the form of use; guidelines for the collection; methods to reduce contamination, preparation, and dilution; and dispensing of the drug (*The United States Homeopathic Pharmacopoeia* 1878).

1. Description of the plant.
   a. Chamomilla. *M. chamomilla*. Feverfew.
   b. This annual is a native of Europe, but is occasionally seen in the flower gardens of this country (United States). It prefers a gravelly soil and grows in both cultivated and uncultivated lands. It is about 2 ft. high, has a branching stem, and bears a profusion of flowers composed of white petals and a yellow disc. Those used officially are imported from Germany.
2. Active principle.
   a. Oleum anthemidis, quercitron, crystallizable principle.
3. Part used.
   a. The whole plant when in flower.

The general practices recommended in the pharmacopoeia for quality, safety, and efficacy are as follows:

1. Collection of plant.
   a. Every plant should be gathered only from those localities to which it is indigenous and their surrounding environmental conditions should be taken into account. If the whole plant is to be used, the most favorable time for gathering is when this is partly in flower and partly in seed.

Collection is prohibited in the rainy season because the oils, resins, volatile principles, and so on, are not secreted during this period.

2. Treatment to reduce contamination.
   a. The plants should be procured whole. Granular and powdered forms should not be used at the initial stage of making the drug as they are prone to adulterants and contaminants. As soon as the plant material is procured, it should be converted into tincture. If a delay is unavoidable, then proper attention should be paid toward wrapping, boxing, and placing the plant in a cool, dry place.
3. Form of preparation.
   a. Tincture, made by macerating one part in five of dilute alcohol for 1 week and by filtering; greenish-brown color; contains the taste and odor of the plant.
4. Preparation of the tincture.
   a. Chamomile tincture is prepared by the method of expression. The plant is cut into very small pieces, it is bruised to pulp in a mortar, then enclosed in a loose muslin bag, and subjected to great pressure as in a screw press. The expressed juice is mixed with an equal part, by weight, of alcohol and allowed to stand in a cool place for 8 days, at the end of which time it is filtered and is ready for use.
5. Dilution of the tincture.
   a. One part of the tincture or solution is mixed with nine parts of the vehicle, which could be water, dilute alcohol, or alcohol. This is strongly shaken or succussed from 100 to 200 times in a vial. The solvents used in dilution such as water should be distilled, and the alcohol should be made nearly anhydrous.
6. Dispensing.
   a. Medicine prepared for homeopathic uses is dispensed in three forms: liquids, powders, and pellets or globules.

1.5.2.3.2 British Homeopathic Pharmacopoeia

The *British Homeopathic Pharmacopoeia* provides a detailed list of common names in addition to the botanical names, a description of the flower, the parts of the plant used, the time for collection, preparation, and forms the drug. In addition, it also specifies measures to ensure the quality of the drugs (*British Homoeopathic Pharmacopoeia* 1876).

1. Description.
   a. Name: Chamomilla.
   b. *M. chamomilla*. Nat. ord., Compositae.
   c. Synonyms: *Chamaemelum vulgare*, *C. nostras*, *Leucanthemum*.
   d. Common names: Wild chamomile, bitter chamomile, corn feverfew.
   e. Foreign names: German, Feld-Kamille, Mutter-Kraut; French, Camomille commun; Italian, Matricaria; Spanish, Matricaria.
   f. Grows in most parts of Europe, in corn fields, waste grounds, and roadsides. Flowers from May to August.

2. Botanical characters.
   a. Receptacle naked, almost perfectly cylindrical, hollow. Very similar to the well-known fetid chamomile (*A. cotula*), but distinguished from it by having no scales on the receptacle.
3. Parts employed.
   a. Whole plant.
4. Time for collecting.
   a. When in flower.
5. Preparation.
   a. Tincture, corresponding in alcoholic strength with 20 OP spirit.
6. Proper forms for dispensing.
   a. Tincture, pilules, or globules.

The *British Homeopathic Pharmacopoeia* also mentions the following measures to maintain the quality, efficacy, and safety of the drug.

1. Water.
   a. The water used for dilution should be the purest. It should not possess color, taste, or smell. Evaporated in a clean glass capsule, it should leave no visible residue.
2. Alcohol.
   a. The alcohol used for dilution should be pure. It should be colorless, transparent, very mobile and inflammable, of a peculiar pleasant odor, and has a strong spirituous burning taste. It should burn with a blue flame, without smoke. With a specific gravity of 0.8298, it should remain clear when diluted with distilled water. Its odor and taste should be purely alcoholic.
3. Plant material.
   a. It should be collected fresh intact, never in the form of powder. When the whole plant is used, it should be gathered when it is partly in flower and partly in seed. In the case of biennials, the collection should be done on the spring of the second year. After the fresh materials are collected, they should be prepared as soon as possible to avoid deterioration. In case of an unwanted delay, the plants should be packed carefully in tin cases (ordinary botanical boxes) and kept as cool as possible.
4. Tincture.
   a. In every instance, the dry crude substance is taken as the starting point from whence to calculate the strength and, with very few exceptions, the mother tinctures contain all the soluble matter of 1 oz. of the dry plant in 10 fl. oz. of the tincture.

1.5.2.4 Quality Issues of Chamomile Homeopathic Formulations

Because the basic starting material of the drug is the chamomile plant, the quality, safety, and efficacy issues of homeopathic formulations are similar to the herbal formulations. These issues are described briefly in Sections 1.5.2.4.1 through 1.5.2.4.4.

1.5.2.4.1 Adulterants

The drugs may contain traces of unsafe starting material, such as the original plant itself may be an adulterant, which can prove toxic (WHO 2009).

1.5.2.4.2 Heavy Metals and Pesticide Residues

There could be contaminants arising from unsafe manufacturing practices as well. Trace amounts of heavy metals and pesticides may be present because of such malpractice.

1.5.2.4.3 Microbial Contamination

Presence of microbes, such as harmful bacteria or fungi, that produce harmful and lethal mycotoxins cannot be ruled out in the drugs.

1.5.2.4.4 Issues of Efficacy

Adverse effects in homeopathy are not expected by homeopaths because of the negligible quantities of active substances in a remedy (Stub et al. 2012). There is a lot of debate on the clinical efficacy of homeopathic medicines (Freckelton 2012). Nonetheless, many consumers, pharmacists, physicians, and other health-care providers continue to use or practice homeopathic medicine and advocate its safety and efficacy (Johnson and Boon 2007). There is a significant body of clinical research including randomized clinical trials and meta-analyses of such trials, which suggest that homeopathy has actions that are not placebo effects (Fisher 2012).

1.5.2.5 Methods to Improve Quality, Safety, and Efficacy of Homeopathic Drugs

The methods to improve the quality of homeopathic medicines involve a combination of the following pharmacopoeial standards and also detection methods to identify adulterants and contaminants. In addition, the packaging of the drugs should strictly follow standard norms. Most of the detection methods are the same as those described for herbal medicines.

1.5.2.5.1 Detection of Adulterants

Because the whole plant of chamomile is used for the preparation of the mother tincture, the original plant material of chamomile should be identified correctly according to the pharmacopoeia or monograph that has the description of the plant. Plants from other adulterant species, if found, should be removed before extracting the juices from the plants.

1.5.2.5.2 Detection of Pesticide Residues

Pesticide residues could be present in the mother tincture of chamomile because of the agricultural practices involved in the cultivation process. These pesticides are potentially harmful and pose safety issues. These pesticides can be detected using the techniques of CC or GC.

1.5.2.5.3 Detection of Heavy Metals

Heavy metals, such as lead or cadmium, and also other metals, such as aluminum, may be present in the mother tincture. These should be detected through techniques such as inverse voltammetry or atomic absorption spectrometry.

1.5.2.5.4 Detection of Microbes

The potentially harmful microbes and mycotoxins that might be present in the mother tincture should be tested using the microbial culture methods and the recommended tests for mycotoxins.

1.5.2.5.5 Detection of Foreign Material

Foreign material that may be present when the plant is being processed to prepare the mother tincture should be carefully removed. These foreign matter could be insects, animal excreta, any other undesirable and toxic matter, and sand. These could be detected visually through the use of microscopes and removed.

1.5.2.5.6 Packaging

The packaging should be done carefully in sterilized containers to ascertain not only the safety of the drug but also the stability and long shelf life of both the package and the drug.

1.5.2.6 Guidelines for Quality, Safety, and Efficacy of Homeopathic Drugs

In 2009, the WHO prepared a technical document on the safety issues of homeopathic drugs with an aim to support the national regulatory authorities—and the manufacturers of homeopathic medicines—in ensuring the safety and quality of homeopathic medicines. The guidelines detailed in the technical document are briefly presented in Sections 1.5.2.6.1 through 1.5.2.6.7 (WHO 2009):

1.5.2.6.1 Identification of Source Material

The source material is the most important aspect of homeopathy. Its correct identification is a must. For this, the WHO specifies the following requirements:

1. Scientific name of the plant
2. Stage of growth
3. Part of plant used
4. Whether cultivated or collected from the wild, and the place
5. Comparison of the specimen with an illustrated description of an authentic specimen for macroscopic and microscopic characteristics
6. Analytical determination of marker substances or standard substances

1.5.2.6.2 Complementary Tests

The complementary tests should be performed on the raw plant material for the following:

1. Foreign matter
2. Total ash

3. Water content
4. Bitterness value
5. Loss on drying
6. Radioactive contamination

1.5.2.6.3 Limit Tests

1. Limit tests should be performed for pesticides, heavy metals, microbes, mycotoxins, and any other relevant matter.
2. Limit tests should be done at the unprocessed or raw stage.
3. Limit tests and ranges should comply with pharmacopoeia standards.

1.5.2.6.4 Mother Tincture

The following data for the mother tincture should be presented, or their absence needs to be justified as follows:

- Method of preparation according to the pharmacopoeia
- Appearance and description
- Identity tests
- Purity tests
- Stability tests

1.5.2.6.5 Finished Product

Homeopathic final products should be tested to determine the following:

- Identity and content
- Quality of dosage
- Residual solvents, reagents, or incidental contamination
- Stability

1.5.2.6.6 Diluents and Excipients

The diluents used in homeopathy, such as the distilled water or alcohol, should be of the pharmacopoeial standards.

The manufacturer should ensure the following:

- All excipients and diluents included in the final product are listed in the documentation and label.
- If new excipients and diluents are included, sufficient data on their safety and quality are provided to national health authorities.

1.5.2.6.7 Labeling

The labeling requirements (among others) are listed as follows:

- Name and address of manufacturer, packager, or distributor
- Manufacturer's batch number
- Content of the product in the container
- Statement that identifies the product as homeopathic

- Scientific name of the active substance, the degree of dilution/potency, and a reference to the pharmacopoeia that was used for the method of preparation
- Indications
- Directions for use and dosage requirements
- Storage conditions
- Warning that advises the user to consult a doctor or qualified health-care professional if the symptoms persist or worsen

1.5.2.7 National Regulations on Homeopathy System of Medicine

Several countries have national laws and regulation in place for the practice, manufacture, and marketing of homeopathic drugs. Some of these are described in Sections 1.5.2.7.1 through 1.5.2.7.3.

1.5.2.7.1 Europe

Homeopathy as a distinct therapeutic system is recognized by law in Belgium (1999), Bulgaria (2005), Germany (1998), Hungary (1997), Latvia (1997), Portugal (2003), Romania (1981), Slovenia (2007), and the United Kingdom (1950) (Camdoc Alliance 2010). In the European Union, the law governing the manufacture and marketing of homeopathic drugs came into force in 2001 under the Directive 2001/83/EC of the European Parliament and of the Council of November 6, 2001 on the Community code relating to medicinal products for human use (Directive 2001).

According to the Article 14 of the Directive, only those homeopathic medicines will be registered for sale, which will have 1 part per 10,000 mother tincture or 1/100th of the smallest dose used in allopathy are administered orally or externally, and no specific therapeutic indication appears on the labeling. There have been several modifications to this Directive. In 2003, the safety issues were brought in the homeopathic medicines in the Directive 2003-63.EC. In the Annexure of this Directive of 2003, in Part III, it is regulated that the quality requirements should be incorporated in the starting material and all intermediate steps of the manufacturing process of the homeopathic drugs. The finished product should be subject to controlled tests and stability tests, and any missing information should be justified (Directive 2003).

In the third amendment of the Directive in 2004, it was stated that if new scientific evidence so warrants, the Commission may amend the third indent of the first subparagraph by the procedure referred to in Article 121(2) (Directive 2004/27). The third indent deals with the dilution requirement of 1/10,000, which is considered unscientific by some researchers and practitioners of medicine.

1.5.2.7.2 United States

The Federal Food, Drug, and Cosmetic Act recognizes the homeopathic drugs and its supplements as official drugs and standards in the Sections 201 (g)(1) and 501 (b), respectively (FDA 1995).The HPUS is also recognized as official under Section 201(j) of the Act, and it is required that the method of preparation of the homeopathic drugs should be according to the HPUS. In addition to the HPUS, there is a compendium to the HPUS, which contains specifications and standards of preparation, content, and dosage of the homeopathic drugs.

According to the Act, in order for a drug to be recognized as homeopathic drug:

1. It should be listed in the HPUS, an addendum to it, or its supplements.
2. The potencies of homeopathic drugs are specified in terms of dilution, that is, 1× (1/10 dilution), 2× (1/100 dilution), and so on.
3. Homeopathic drug products must contain diluents commonly used in homeopathic pharmaceutics.

To maintain the quality of homeopathic drug, labeling containing all the specifications is mandatory. The labeling is categorized for prescription drugs and over-the-counter drugs.

The General Labeling Provisions should include the following:

1. Name and place of business of the manufacturer, packer, or distributor.
2. Directions for use (not for prescription drugs).
3. Statement of the quantity and amount of ingredient(s) expressed in homeopathic terms, for example, l× and 2×.
4. Documentation must be provided to support those products or ingredients that are not recognized officially in the HPUS.
5. Established name that may include both English and Latin names.

1.5.2.7.2.1 Prescription Drugs

The products must comply with the general labeling provisions mentioned previously. In addition, the label should have a drug legend that says "Caution: Federal law prohibits dispensing without prescription," a statement of identity and a declaration of net quantity of contents and statement of dosage.

1.5.2.7.2.2 Over-the-Counter Drugs

Product labeling must comply with the general labeling provisions mentioned previously. In addition, it should have a principal display panel, statement of identity, declaration of net quantity of contents, indications for use likely to be understood by lay persons, directions for use, and warnings.

1.5.2.7.3 India

The manufacture and marketing of the homeopathic drugs in India are regulated by the Drugs and Cosmetics Act, 1940.

Section 2 (dd) of the Act specifies what drug is considered homoeopathic medicines. According to the Act, a drug is considered as homeopathic medicine if it meets the following criteria:

1. It is recorded in *Homoeopathic Pharmacopoeia*.
2. Its therapeutic efficacy has been established through long clinical experience as recorded in authoritative homoeopathic literature of India and abroad.
3. It is prepared according to the techniques of homoeopathic pharmacy.
4. Covers combination of ingredients of such homoeopathic medicines but does not include a medicine that is administered by parenteral route.

In 1973, The Homeopathy Central Council Act, 1973 (India) was enacted to provide for the constitution of a Central Council of Homoeopathy and maintenance of a Central Register of Homoeopathy and for matters connected therewith. In 2003, the Department of Ayurveda, Yoga and Naturopathy, Unani, Siddha, and Homoeopathy (AYUSH) was established, which deals with the education and practice of homeopathy, the manufacture and formulation of homeopathic drugs, and their marketing.

Subsequent amendments in the Drugs and Cosmetics Act, 1940 incorporated the issues of the quality, safety, and efficacy of the homeopathic drugs. The Section 3(7) of the Act specifies that testing of the homeopathic drugs should be carried out in the designated national laboratories.

There are provisions to ensure the quality, safety, and efficacy of the drugs, which are manufactured in India or those that are imported and sold in the Indian market. This is provided in the Second Schedule of the Act (The Drugs and Cosmetics Act 1940, p. 49) and presented below.

1. Drugs included in the *Homoeopathic Pharmacopoeia of India*. The standards required for the drugs manufactured according to the *Homeopathic Pharmacopoeia of India* are the following:
   a. The label should display the list of ingredients.
   b. Standards of strength, quality, and purity, as may be prescribed.
2. Drugs not included in the *Homoeopathic Pharmacopoeia of India*, but which are included in the *Homoeopathic pharmacopoeia of the United States* or *the United Kingdom*, or the *German Homoeopathic Pharmacopoeia*: For such drugs, the standards of identity, purity, and strength prescribed in such pharmacopoeia and other standards as may be prescribed should be followed.
3. Drugs not included in the *Homoeopathic Pharmacopoeia of India, the United States*, or *the United Kingdom*, or the *German Homoeopathic Pharmacopoeia*: For such drugs, the label should display the formula of list of ingredients and such other standards as may be prescribed by the central government should be followed.

1.5.2.7.3.1 Conditions of License

The marketing of homeopathic drugs in India as per the Section 67 (A) of the Drugs and the Cosmetics Act, 1940 require licenses that are issued by the government after stringent scrutiny. The license is granted after ensuring that the premises in which the drugs are manufactured and stocked are clean and hygienic. The following conditions are specified in the Section 85 H (e) of the Act with relation to the quality, safety, and efficacy of the mother tincture:

1. Crude drug used shall be identified.
2. Alcohol content shall be determined.
3. Containers should be of clean, neutral glass.
4. Hygienic conditions shall be scrupulously observed during the manufacturing process.

The Section 88 of the Act also specifies the labeling of containers. The label of the container should have the following information:

1. Name and address of the manufacturer
2. Scientific name of the substance
3. Purpose for which it has been manufactured

1.5.3 Unani System of Medicine

The Unani system works under the principle that disease is a natural process and the symptoms are the reactions of the body to the disease. The Unani system of medicine originated in Greece and was developed by the Arabs. Buqrat (Hippocrates) is known to be the father of this system of medicine, and the contribution of Jalinus (Galen) is significant. Ibn Sina (Avicenna) was a physician of this system whose work Al-Quanoon (Canon of Medicine) is one of the most important medical books for more than six centuries (NFUM 2006; Unani Formulations 2012). The Unani system of medicine is practiced widely in the Arabian countries as well as in Indian subcontinent under various names such as Greco Arab Medicine, Arabic Medicine, Tibb-e-Sunnati, Traditional Iranian Medicine, Eastern Medicine, and Uighur Medicine.

Over the centuries, the Unani system has imbibed the traditional medicines prevalent in Egypt, Syria, Persia, India, Middle East, Far East, and Central Asian countries (NFUM 2006). Therefore, it follows a combination of several working principles of the body including the hippocratic principles of humors, which are Dam (Blood), Balgham (Phlegm), Safra (Yellow bile), and Sauda (black bile) (Rahman et al. 2008). The drugs used in Unani are of herbal, animal, or mineral origin. The herbal drugs are single-origin drugs or compound formulations. The drugs are taken internally or applied externally. Internally the drugs may be taken as tablets, pills, and powders. For external use, the drug formulations are made as ointments and medicated oils (Kabir 2003).

Chamomile is called Babuna in the Unani system of medicine. It is used as a single drug or as a compound formulation with other components. The temperament (Mijaz) of the drug is hot and dry. The mode of administration is oral or local and as directed by the physician. It is used as a dilator, demulcent, resolvent, diuretic, emmenagogue, abortifacient, relaxant, brain tonic, and expectorant.

1.5.3.1 Disease Conditions

The various disease conditions in which chamomile is recommended are distension, headache, cold, stomatitis, conjunctivitis, scabies, itch, jaundice, real stones, fever, ileus, cystalgia, and herpes cornea. The reference to this drug and its use for treating the disease conditions can be traced back to the Al-qanun Fil-tibb, Vol II by Abu Ali Ibn Sina in the eleventh century. Some other disease conditions in which Babuna is used have been compiled in Table 1.6.

1.5.3.2 Formulations of Chamomile

In the Indian subcontinent, the Unani system of medicine uses chamomile as an ingredient in several of its formulations (Ali 1979). The different forms of chamomile formulations used in Unani medicines are the ointments (majoon, jawarish,

TABLE 1.6
Disease Conditions under Which Chamomile Is Recommended in the Unani System of Medicine

S. No.	Disease Conditions
1.	Indigestion
2.	Polyuria
3.	Anorexia
4.	Dementia
5.	Amnesia
6.	Sexual debility
7.	Dysuria
8.	Rheumatism
9.	Swelling(s)
10.	Visceritis
11.	Lumbago
12.	Earache
13.	Pneumonia
14.	Anterior mesodmitis
15.	Mediastinal pleurisy

Source: NFUM, *National Formulary of Unani Medicine,* Central Council for Research in Unani Medicine, India, 2006; Rashid, M.A. and Ahmad, F., *Hamdard Medicus,* 37, 73–81, 1994.

zimad, and qairooti) and the medicated oil (Raughan) (Rashid and Ahmad 1994; NFUM 2006). Their form and method of preparation are described below:

1. Majoon: It is a semisolid preparation of the dried chamomile flower in an edible base. The base is prepared by adding purified honey, sugar, or jaggery to water and boiling over a slow fire. After it acquires the required consistency, the base is purified by adding lime juice and alum. The powdered drug is mixed with a little clarified butter (ghee) and added to the base to produce a semisolid preparation. The majoon is taken internally.
2. Jawarish: It is a type of majoon but with a few differences. Its base is semisolid but of more liquid consistency than majoon. Another difference is that the powdered drug is coarser than majoon.
3. Zimad: The powered form of the drug is called zimad. The dried flowers are finely powdered and passed through a sieve of 100 mesh size. The powder is added to heated wax and then cooled. The product zimad is in the form an ointment (Marham), which is applied externally.
4. Qairooti: It is a semisolid preparation, just like an ointment. It is used externally. To prepare qairooti, the oils (Raughan-e-badam, Raughan-e-gul, or any other oil mentioned in the text) are heated and then wax or fat is dissolved in the oils. The dried chamomile flowers are mixed and stirred until a semisolid mass is formed.

5. Raughan-e-Babuna: The dried chamomile flowers are steeped in an appropriate oil to prepare raughan (oil). Such a type of preparation is made by the following method: 4 parts (by weight) dried flowers are soaked in 5 parts (by weight) of sesame and kept in a covered glass jar. This jar is exposed to sunlight for 40 days. The material is taken out after 40 days and crushed with hands to obtain a thorough suspension. The suspension is filtered using a fine cloth. The medicated oil obtained is used externally.

Table 1.7 lists the different Unani formulations and their forms, methods of administration, therapeutic uses, and the mechanisms of actions (Unani Formulations 2012).

In addition to the formulations mentioned in Table 1.6, some other formulations available in the market are listed as follows (NFUM 2006):

1. Majoon-e-Hafiz-ul-Ajsad
2. Qairooti Babuna Wali
3. Qairooti-e-Arad-e-Baqla

TABLE 1.7
Different Formulations, Forms, Administration, and Action of Chamomile Drugs in the Unani System of Medicine

S. No.	Formulation	Form of Drug	Form of Administration	Action of Drug
1.	Jawarish Baboonah	Semisolid	Oral	Stomachic
2.	Majoon-e-Falasifa	Semisolid	Oral	Stomachic, digestive, appetizer, sedative
3.	Zimad-e-Muballil-ut-Teeb	Ointment	Topical	Anti-inflammatory
4.	Zimad-e-Sumbul-ul-Teeb	Ointment	Topical	Anti-inflammatory
5.	Raughan-e-Babuna-Sada	Oil	Topical	Analgesic, anti-inflammatory
6.	Raughan-e-Babuna-Qawi	Oil	Topical	Analgesic, anti-inflammatory
7.	Dawa-e-Waja-ul-Ain	Tablets, pills, powder, decoction, paste	Oral	Severe pain of the eyes
8.	Nutool Barai Tahabbuj	Liquid	Poured on affected part	Edema
9.	Majoon-e-foodanaj	Semisolid	Oral	Antipyretic, cold
10.	Inkebab	Vapor	Inhalation	Headache
11.	Raughan Nardin	Oil	Topical	Coldness of stomach, colic
12.	Majoon-e-Atiyatullah	Semisolid	Oral	Piles, hemorrhoids

4. Qairooti-e-Mamool
5. Zimad Kharateen Shingrafi
6. Zimad Muqawwi
7. Zimad Niswan
8. Raughan Muqawwi-e-Asab
9. Raughan Samaat Kusha Jadeed
10. Bekh-e-Babuna
11. Tukhm-e-Babuna

1.5.3.3 Unani Pharmacopoeia

The Unani pharmacopoeia describes chamomile as Babuna. In fact three separate descriptions are provided for Babuna, Gul-e-Babuna, and Tukhm-e-Babuna as follows:

1. Babuna (*The Unani Pharmacopoeia of India* 2009)
   a. Babuna is a crude drug comprising chamomile flowers.
   b. Name: *M. chamomilla* L. of Asteraceae
      i. Morphology
         A. Peduncles: 0.20–0.40 cm in diameter, 1.5–2.0 cm long
         B. Receptacle: Discoid with involucral bracts
         C. Sepals: Pappus with brown margins
         D. Petals: Ligulate, white, elongate, tridentate
         E. Androecium: Stamens with short filament, epipetalous, and connate
         F. Gynoecium: Ovary bicarpellary, syncarpous, unilocular
         G. Seed: Anatropous, black, single in each ovary on basal placentation, vertically three to five ribbed
      ii. Chemical
         A. Total ash: Not more than 7.50%
         B. Acid-insoluble ash: Not more than 1.55%
         C. Alcohol-soluble matter: Not less than 12.00%
         D. Water-soluble matter: Not less than 20.00%
2. Gul-e-Babuna
   a. Gul-e-Babuna consists of the floral shoots of chamomile
   b. Name: *M. chamomilla* L. of Asteraceae
      i. Cellular
         A. Petal: The transverse section has uniseriate, adaxial, and abaxial epidermal layers containing unicellular covering hair; sandwiching homogenous parenchymatous mesophyll, few cells containing cuboid or rhomboid calcium oxalate crystals
         B. Anthers: Dithecous, tetralocular anther lobes, obtuse, entire pollen grains globular, tectum smooth, 5–6 μm in diameter
         C. Ovule (seed): Unitegmic, albuminous
3. Tukhm-e-Babuna
   a. Description provided is the same as Gul-e-Babuna.

1.5.3.3.1 Dosage

1. The doses, unless otherwise stated are regarded suitable for adults when administered orally two to three—times in 24 hours. The frequency and the amount of the therapeutic agent will be the responsibility of the medical practitioner.
2. If in case of administration of the drug by a route other than oral, the single dose for such administration is mentioned.

The Unani pharmacopoeia provides not only the description of the plant but also several single and compound formulations of chamomile, such as Raughan-e-Babuna (single drug), and Majoon-e-Falasifa (compound formulation). But most importantly, it provides the methods for testing the samples of the formulations in Appendices 1–5 of the pharmacopoeia. Appendix 1 specifies the apparatus to be used for the tests of the samples. The use of weights and measures, volumetric glassware, sieves, and so on are specified. Appendix 2 specifies the methods to determine microbial contamination and also the determination of quantitative data, such as foreign matter, total ash, volatile oil content, TLC, and alkaloid estimation. The Appendix also specifies limit tests for arsenic, heavy metal and pesticide contamination, and GC. Appendix 3 specifies physical tests such as those for determining the refractive index. Appendix 4 specifies the reagents and solutions. Appendix 5 specifies estimations of tannins and determination of elements such as aluminum or mercury.

1.5.3.4 Quality Issues of Unani Formulations

The quality issues of the Unani medicines are similar to the quality issues of the herbal formulations of traditional medicine since the starting material is a plant. The flowers could be adulterated with flowers from other plant species (Joharchi and Amiri 2012) or contaminated with pesticides, heavy metals, or microbes during cultivation or postharvest handling. Quality issues are present regarding the efficacy of the drug formulations (Rahman et al. 2008). Quality issues also arise during the manufacturing and storage of the drugs. Further, the issues of quality arise when the drug is marketed.

1.5.3.5 Quality Control of Unani Formulations

The National Formulary for Unani medicine and the Unani pharmacopoeia has laid down specifications for standardized formulation of Unani drugs. The Unani pharmacopoeia has extensively described the methods that are to be followed to ensure the manufacture of quality Unani formulations.

1.5.3.5.1 Formulations

The process of preparation of the formulations has been standardized by the National Formulary of Unani Medicine, Ministry of Health and Family Welfare, Government of India, based on authentic Unani literature (NFUM 2006).

1.5.3.5.2 Purity

For drugs originating from plants, they should be free from the following (NFUM 2006, pp. xxix–xxx):

1. Insects, foreign matter, animal excreta, fungus growth, mold, or other evidence of deterioration (toxic, injurious, or harmful) and to show no abnormal substances, odor, color, or sliminess.
2. Any unnatural and unusual impurity for which the rational considerations require that it be absent and it should not be putrefied or decomposed form.

The National Formulary specifies that the foreign impurities in drug should be cleaned by sieving or washing.

1.5.3.5.3 General Process of Preparation

1.5.3.5.3.1 Grinding

The general process of drug preparation involves making a powder of the chamomile drug. The particle has to be of a specific mesh size. The process of making the powder involves grinding in a mortar and pestle, made of stone, iron, wood, porcelain, or glass. Sometimes they are rubbed on a flat grinding stone.

1.5.3.5.3.2 Washing

In some preparations, the chamomile flowers are not powdered but directly used. These flowers are washed for a few hours before the formulation is prepared.

1.5.3.5.4 Specified Precautions to Be Observed during Preparation

1. Pills and tablets
   a. The pills or tablets are made by taking a small mass and mixed with a water-soluble adhesive. A weighed amount of this mass is taken and rolled between the fingers. Specific oils are used during rolling the mass to avoid sticking of the mass to the fingers. It is specified that the pills and tablets should neither be too hard nor too soft. The tablets are to be preserved carefully in clean, well-dried jars and stored in a cool and dry place to avoid contamination.
2. Ointment (Majoon)
   a. The majoon is prepared by mixing one component with another. During its preparation, care should be taken to stir continuously to allow proper mixing. The mixture should not come in contact with moisture under any condition. The majoon is recommended to be preserved in dried and clean glass, china clay, or tin-coated special containers. During preservation, if the majoon gets dry, it can be brought to normal consistency by adding purified honey or a thick syrup made of sugar.
3. Medicated oil (Raughan)
   a. The process of extraction should be strictly according to the "General Methods of Preparation." The oil should always be of the required consistency, flavor, color, and tests as given in the Unani texts. These oils

should be preserved in clean and dry glass jar containers under hygienic conditions in a cool and dry place.

1.5.3.5.5 Storage

1. Container and its cover must not interact physically or chemically with the substance that it holds so as to alter the strength, quality, or purity of the substance.
2. Container should be tight and well closed. It should protect the contents from contamination, moisture or extraneous solid, efflorescence, deliquescence or evaporation, and loss of substance under ordinary or customary conditions of handling, shipment, storage, or sale.

1.5.3.6 National Legislation in India

The Unani formulations are manufactured and marketed as per the regulations of the Drugs and Cosmetics Act, 1940, as amended in 1964, and the Drugs and Cosmetics Rules, 1945 (The Drugs and Cosmetics Act 1940). The Act has defined a Unani drug and laid the regulations for marketing quality, safe, and effective Unani drugs. In this Act, a Unani drug is defined as a drug, which includes all medicines intended for internal or external use in the diagnosis, treatment, mitigation, or prevention of diseases in accordance with the formula described in the authoritative books of Unani (Tibb) systems of medicine. The Act also specifies misbranded, spurious, and adulterated drugs. According to the Act, a Unani drug shall be deemed to be adulterated if

- It consists of any filthy, putrid, or decomposed substance.
- It has been prepared, packed, or stored under insanitary conditions.
- Its container is composed of any poisonous or deleterious substance.
- It bears or contains a color other than one that is prescribed.
- It contains any harmful or toxic substance.
- Any substance has been mixed therewith so as to reduce its quality or strength.
- It has been substituted wholly or in part by any other drug or substance.

The Drugs and Cosmetic Rules of 1945 provides proper labeling of the Unani drugs.

1.5.3.6.1 Labeling

The label of the drug should contain the following information, among others:

1. Name of the drug
2. Reference to the method of preparation thereof as detailed in the authoritative books
3. Correct statement of the net content in terms of weight, measure, or number
4. Name and address of the manufacturer
5. Number of the license under which the drug is manufactured
6. Batch number

7. Date of manufacture
8. Words "Unani medicine."
9. Words "FOR EXTERNAL USE ONLY" if the medicine is for external application

To fulfill the objectives of the Drug and Cosmetics Act, 1940, the Government of India set up the pharmacopoeia committee for Unani medicine in 1964. In 1970, a Pharmacopoeial Laboratory for Indian Medicine was established to work for evolving standards for Unani drugs. In 1981, as a result of extensive deliberations by the Unani Pharmacopoeia Committee, *National Formulary of Unani Medicine* was compiled. Following this, in 2009, *The Unani Pharmacopoeia of India* was compiled, which comprises hitherto unstudied and unreported standards for single drugs of plant origin included in the *National Formulary of Unani Medicine*.

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