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PHYTOCHEMISTRY AND PHARMACEUTICAL EVALUATION OF *Balanites aegyptiaca*: AN OVERVIEW

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KEYWORDS

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Secondary Metabolites

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ABSTRACT

Balanites aegyptiaca, is one of the awfully potent neglected wild plant species found mainly in both African and South Asian deserts. It is a historical and elegant folkloric medicinal plant due to its curative nature towards diverse fatal diseases, it is conventionally utilized in management of a variety of ailments such as jaundice, intestinal worm infection, wound healings, malaria, syphilis, epilepsy, dysentery, stomach aches, constipation, diarrhea, haemorrhoid and asthma. Biochemical analysis of plant extract revealed the presence of carbohydrates, lipids, proteins, alkaloids, flavonoids, saponins and organic acids. Due to the presence of these active ingredients, it is served as antioxidant, antihelminthic, antimicrobial (mainly the fixed oil) immunostimulant, anticarcinogenic, antidiabetic, contraceptive antifeedant, antiviral and molluscicidal activities. In conclusion, this review explored the presence of various secondary metabolites from various plant parts of *Balanites aegyptiaca.*

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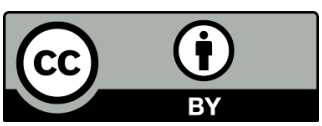

1 Introduction

Balanites aegyptiaca (L.) Delile, a drought-tolerant perennial tropical ever green tree belongs to family Zygophyllaceae (Balanitaceae), is commonly known as 'desert date' (Heiglige in Arabia) (Hall & Waljer, 1991). The name Balanites originally derived from the Greek word which means fruit resemble acorn (Gupta et al., 2012). It is also known by different vernacular names such as as Angarvriksha, Balanite, Desert date, Bedeno, Hingot, Soapberry tree, Thorn tree and Egyptian balsam and many more (Rathore et al., 2005). It is native to arid and sub arid part of Africal and Middle East especially Arabian Peninsula (Arboneir, 2004) but most widely in various parts of Africa and South Asia (Hall & Waljer 1991; Ndoye et al., 2004; Hammouda et al., 2005; Okia et al 2011; Chothani & Vaghasiya, 2011; Al-Thobaiti & Abu Zeid, 2018). Presence of tree is well reported from India, Iran, Pakistan (Amalraj & Shankarnarayan, 1998), Sudan (Grosskinsky & Gullick, 2001), Nigeria (Lockett et al., 2000), Ethiopia, (Guinand & Lemessa, 2001; Aregay et al., 2017), Ghana (Augustus et al., 2014), and Burkina Faso (Sourabie et al., 2013).

It can be grow in various habitat, soil types and climatic conditions (Varshney & Vyas, 1982; Sarker et al., 2000; Pandey, 2005). Also, the tree has good adaptive mechanisms to grow and thrive under combined water and salinity stresses (Maksoud & El-Hadidi, 1988). It is a multi branched, thorny, shrub or tree which reached upto 10 m in height (Yadav & Panghal, 2010; Chothani & Vaghasiya, 2011). In the month of October, the tree has inflorescence bearing yellow-green bisexual flowers which exude nectar.

B. aegyptiaca is multipurpose tree and used for food and fodder in almost all parts of Africa and South Asia (Elseed et al., 2002; Billore, 1988). Among the various plant parts, fleshy pulp of the fruit is eaten fresh or dried. It also used as a food, beverage, & medicines (National Research Council, 2008). In protein content, this fruit is superior than banana, guava, mango and papaya. Fleshy fruit contains 64 – 72% carbohydrates, crude protein, steroidal saponins (Dawidar & Fayez, 1969), vitamin A, vitamin C and other essential minerals for human. Seed kernel also widely used for oil. The kernel produces high quality edible oil (Obidah et al., 2009) with large number of medicinal properties (Hanan et al., 2009). The kernel is also rich in protein and minerals contents (Elfeel & Warrag, 2011). In quality aspect, it is similar to sesame and groundnuts oils (Abu Al-Futuh, 1983; Obidah et al., 2009). Seed also used for biodiesel production (Chapagain et al., 2009; Gutti et al., 2012; Kumawat et al., 2012).

Different parts of *B. aegyptiaca* have several bioactive substances which possess miscellaneous medicinal properties. A bioactive substance is defined as a constituent possessing an effect on causes of a reaction, or trigger of a response in the living tissue (Abdelkarim et al., 2014). The bark, fruit and oil of tree have been widely used to treat various disease or disorders such as cancer (Gnoula et al., 2008; Hassan et al., 2016; Montasser et al., 2017), tuberculosis (Hassan et al., 2016), HIV/AIDS (Sheded et al., 2006; Alashaal et al., 2010), malaria (Kusch et al., 2011; Bobbo et al., 2016; Sibhat & Hiben, 2016), diabetes (Helal et al., 2013; Abou Khalil et al., 2016), sleeping sickness (Barley, 1962; Sheded et al., 2006; Alashaal et al., 2010), wounds (Chevallier et al., 2003; Kommu et al., 2013), colds, syphilis, liver and spleen disorders (Abdel-Kader et al., 2008; Zaahkouk et al., 2015), jaundice (Sarker et al., 2000; Abdulmalik et al., 2011), yellow fever, snake bite (Ojo et al., 2006) and aches (Mohamed et al., 1999; Hamid et al., 2001). The infusion of root bark has been used in diarrhoea, haemorrhoid and also acts as a fish poison (Bukar et al., 2004).

B. aegyptiaca fruits have various primary and secondary metabolites such as flavonoids, furanocoumarin, saponins, fixed oil protein, fat, carbohydrates and vitamin C. Along with this it has various electrolytes or minerals such as calcium ions, iron, magnesium, phosphorus, zinc, copper and potassium ions (Stadlmayr et al., 2013). Among the identified secondary metabolites, anticancer or anti tumors properties of Balanitin and saponins has been well reported by various researchers (Gnoula et al., 2008; Hassan et al., 2016)

2 Objective of Review

This review focus on the ethnopharmacological potential and phytochemicals present in different parts of *B. aegyptiaca* with beneficial health effects. Though already some information are available on the phytochemical constitution of *B. aegyptiaca* and its effect on human health but up-to-date and critical information on the plant with respect to its ethnopharmacology and phytopharmaceutical potential is scanty and not well-documented. Therefore, this review has been written on various aspects of ethnopharmacology and phytochemistry of *B. aegyptiaca*.

3 Phytochemical Constituents of *B. aegyptiaca*

B. aegyptiaca have been investigated chemically for various classes of constituents. It is reported to contain a number of secondary metabolites and bioactive compounds (Figure 1- 4), including flavonoides, alkaloid, glucosides, phenolic, steroids saponins, furanocoumarins, Diosgenin, N-trans-feruloyltyramine, N-cis-feruloyltyramine, trigonelline, balanitol, fatty acid (Speroni et al., 2005).

3.1 Flavonoids

Flavonoids consist of two aromatic carbon rings viz., benzene and benzopyran, based on the arrangement of carbon ring oxidation degree (Spencer, 2008). Presence of the various class of

flavonoids has been reported from the *B. aegyptiaca*c, among these some important classes of flavonoids viz., quercetin-3-rutinoside, quercetin 3-glucoside, 3-glucoside, 3-rutinoside, 3-7-diglucoside and 3-rhamnogalactoside of isorhamnetin have been extracted from the leaves and fruit of the *B. aegyptiaca* (Maksoud & El-Hadidi, 1988; Sarker et al., 2000). Speroni et al. (2005) have been identified the presence of Isorhamnetin-3-O-robinobioside from all parts of *B. aegyptiaca*. *B.* Flavonoids have considerable role in tumour and chronic disease treatment and also have antimicrobial properties (Salwa et al., 1988; Samuelsson et al., 1991; Kamel, 1998, Speroni et al., 2005).

3.2 Alkaloids Compounds

B. aegyptiaca bark contains various alkaloids such as N-trans-feruloyltyramine and N-cisferuloyltyramine. Presence of the alkaloids has been also reported from the seeds and oil. Role of N-trans-feruloyltyramine in cancer treatment have been well studied by various researchers (Sarker et al., 2000).

3.3 Steroidal Glycosides

Farid et al. (2002) isolated five steroidal glycosides viz., (3β,12α,14β,16β)-12-hydroxycholest-5-ene-3, 16-diyl bis(β-D-glucopyranoside) , (3β,20S,22R,25R)- and (3β,20S,22R,25S)-26-(β-D-glucopyranosyloxy)-22-methoxyfurost-5-en-3-yl β-D-xylopyranosyl-(1→3)-β-D-glucopyranosyl-(1→4)[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside, (3β,20S,22R,25R)- and (3β,20S,22R,25S)-spirost-5-en-3-yl β-D-xylopyranosyl-(1→3)-β-D-glucopyranosyl-(1→4)[α-L-rhamnopyranosyl-(1→2)]-β-D-glucopyranoside from *B. aegyptiaca* roots (Hostettmann & Marston, 1995).

Presences of various types of saponins have been reported from *B. aegyptiaca* crude extract. Saponins are complex association of glycosides (Sugar residues) and sapogenin (aglycone part of 27–31 carbon atoms as steroid or a triterpene). Major steroidal saponins which have been reported from bark and root of *B. aegyptiaca* are balanitin -1, 2, 3, 4, 5, 6 and 7 (Hardman & Sofowora, 1970; Morsy, 2008; Gnoula et al., 2008). Recently saponins proved to have wide range of medicinal properties such as anticancer or antitumor (Gnoula et al., 2008), anti-inflammatory properties, inhibitory effect on HIV, antioxidant activity (Ali et al., 2012), effective antischistosomal remedy (Koko et al., 2005), and mosquito control (Wiesman & Chapagain, 2003).

Diosgenin is a type of sapogenin compound which have been isolated from seed, leaves and fruit of *B. aegyptiaca*, and can be used as natural source of steroidal hormones (FAO, 1985; Pettit et al., 1991; Farid et al., 2002). According to Beneytout et al. (1995) and Nappez et al. (1995) diosgenin is responsible for morphological and biochemical changes in megakaryocyte cells. Hosny et al. (1992) reported the presence of 6-methyl diosgenin from the fruit of *B. aegyptiaca*.

Preliminary phytochemical investigations revealed that *B. aegyptiaca* possessed various classes of glycosides such as cardiac glycosides, Balanitoside, Pregn-5-ene-3β,16β,20(R)-triol 3-O-β-d-glucopyranoside and 26-(O-β-D-glucopyranosyl)-3-β-[4-O-(β-D-glucopyranosyl)-2-O-(α-L-rhamnopyranosyl)-β-D-glucopyranosyloxy]-22,26-dihydroxyfurost-5-ene (Kamel & Koskinen 1995; Speroni et al., 2005; Staerk et al., 2006; Al Ashaal et al., 2010; Chothani & Vaghasiya, 2011). The roots and bark also contain yamogenin which is a glycone with a branched glucose and rhamnose side chain (Speroni et al., 2005). These phytochemicals may be responsible for the treating certain skin infections, heart disease and diabetes (Chothani & Vaghasiya, 2011). Yamogenin have properties to cure hepatic steatosis, diabetic mellitus and obesity (Speroni et al., 2005).

3.4 Glucosides

The leaves, fruit, bark and kernels of *B. aegyptiaca* were found to contain various class of glucosides including 2-Diglucosyldirhamnoside, beta-sitosterol, di-, tri-, and tetraglucosides. These glucosides are responsible for the antidiabtic and antimicrobial properties of the tree extract (Varshncy & Vyas (1982); Saeed et al., 1995; Kapseu et al., 1997; Ansari et al. 2006; Breimer et al., 2007).

3.5 Phenolic Compounds

The bioactive constituent's phenols are reported from seeds and bark of *B. aegyptiaca*. Most commonly reported phenolic compounds are 2,4-di-tertbutyl-phenol, 2,6-di-tert-butyl-phenol (seed), 3-hydroxy-1-(4-hydroxy-3- methoxyphenyl)-1-propanone, syringic acid, vanillic acid and Coumarins (bark). These phenolic compounds have antimalarial, antioxidant, anti-diabetic, antiinflammatory, anti-tumor, enzyme inhibitory antifungal, antimicrobial and antiviral, activity (Sarker et al., 2000; Kusch et al., 2011; Rohini & Srikumar, 2014).

3.6 Fatty Acid

The seed oil of *B. aegyptiaca* is good and edible quality with highest percentage of Fatty acids. The oil contains mainly palmitic, stearic, oleic, and linoleic acids which were the main

fatty acids (Zang et al., 2017). Presence of Omega-3 and Omega-6 Essential Fatty Acids from kernel seed oil has been reported by Elhardallou et al. (2014). The oil exhibited anticancer activity against lung, liver, and brain human carcinoma cell lines. It also had antimutagenic, antiviral and antimicrobial activities against the selected microorganisms.

3.7 Other Compounds

In addition to the above phytochemicals, presence of 1-10-methyl-n-heptacosane (Ansari et al., 2006), balanitol (Cordano et al., 1978), bergapten (Seida et al., 1981; Breimer et al., 2007), cryptogenin, deltoin (Speroni et al., 2005), furanocoumarin (Khare 2007) and marmesin (Ansari et al. 2006; Breimer et al., 2007) has been reported from the bark of *B. aegyptiaca*. Presence of Protodeltoin (Speroni et al., 2005) and 6-phenyl-2(H)-1,2,4-triazin-5-one oxime (Kusch et al., 2011) has been reported from the seed of *B. aegyptiaca*. These chemicals also have antioxidants, antimalarial, anti-inflammatory and antidiabtic properties (Speroni et al., 2005; Ansari et al. 2006; Breimer et al., 2007; Kusch et al., 2011). Psoriasis treatment capability of bergapten has been reported by Ansari et al. (2006) and Breimer et al. (2007).

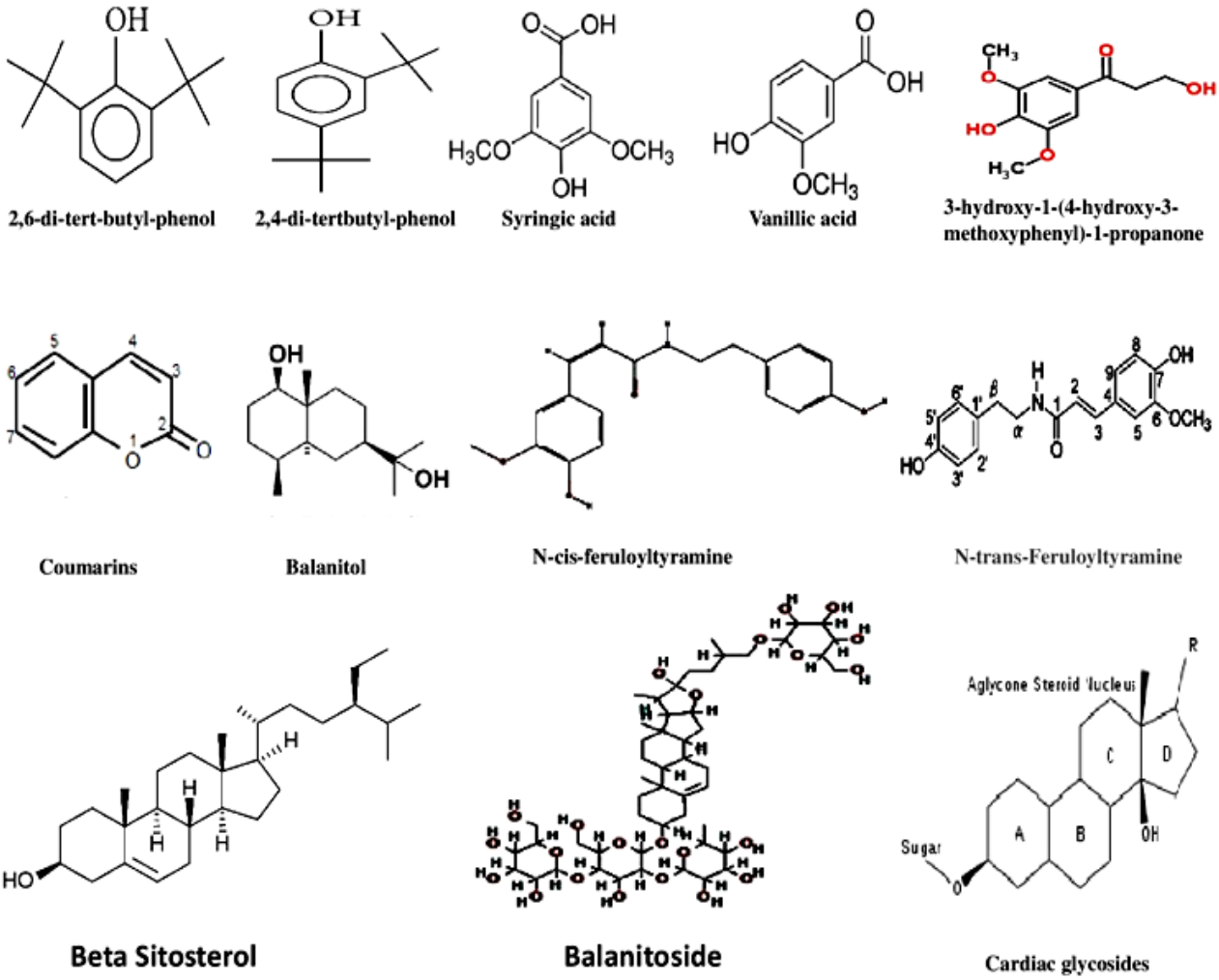

Figure 1 Chemical identified and isolated from *Balanites aegyptiaca*

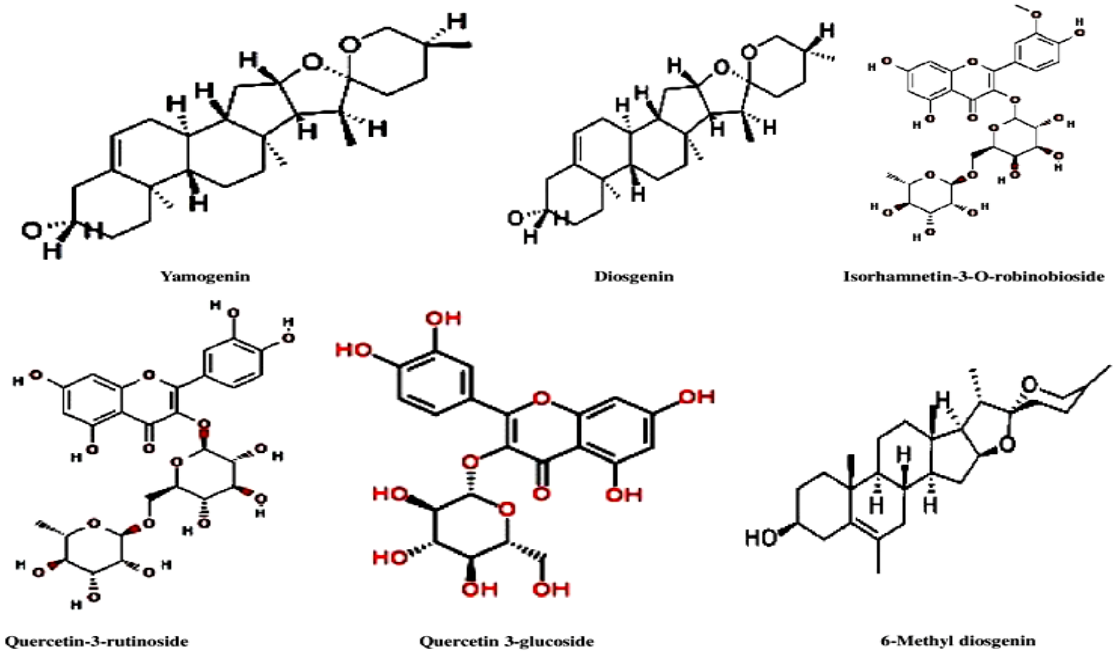

Figure 2 Chemical identified and isolated from *Balanites aegyptiaca*

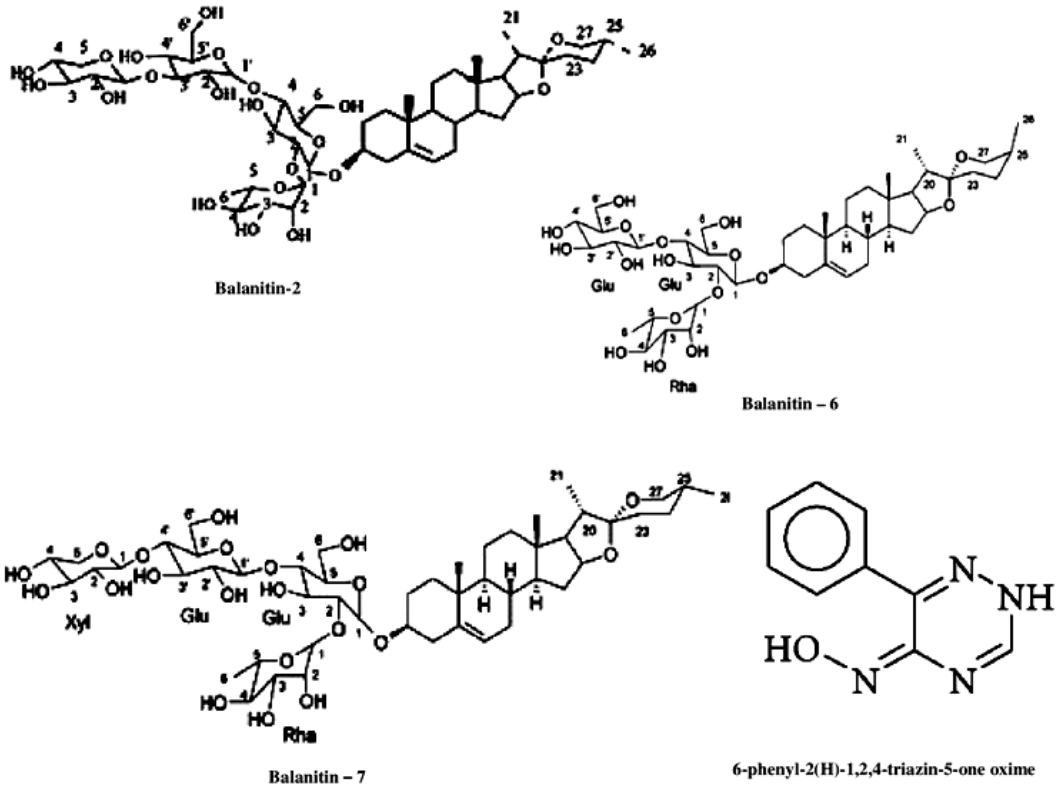

Figure 3 Chemical identified and isolated from *Balanites aegyptiaca*

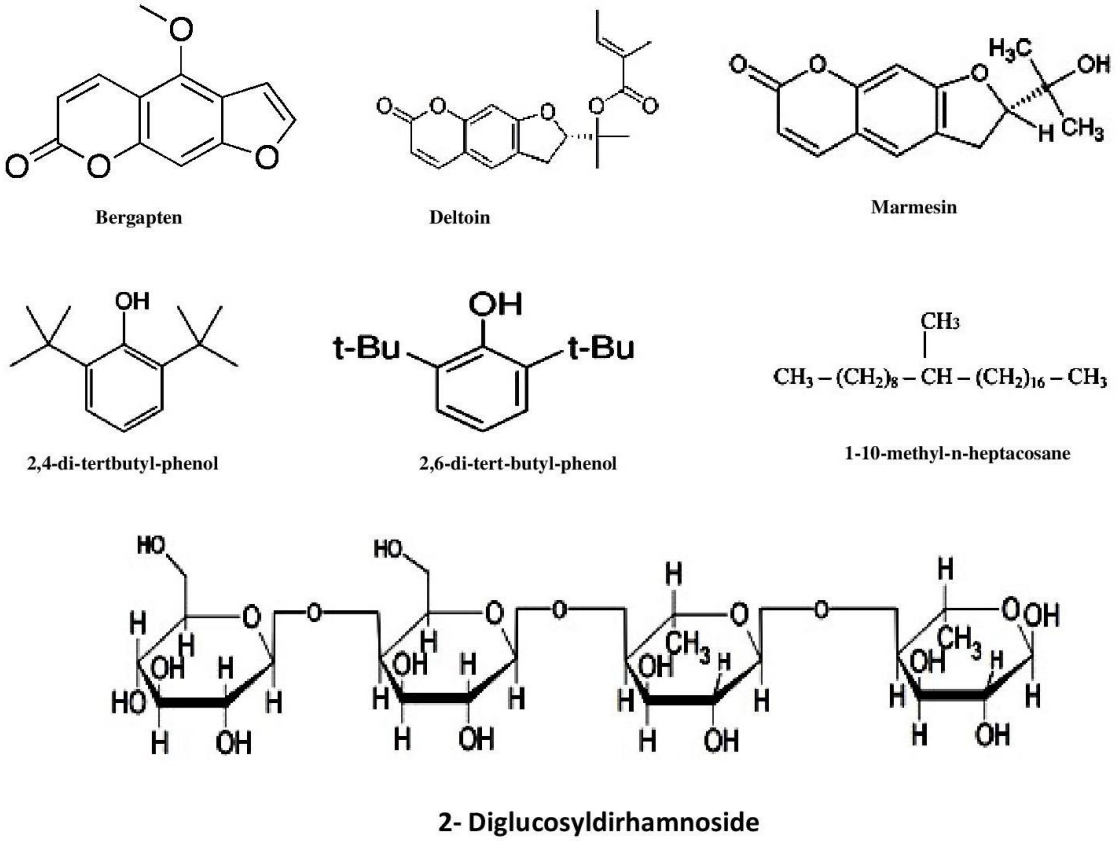

Figure 4 Chemical identified and isolated from *Balanites aegyptiaca*

4 Pharmacological Aspects of Isolated metabolites

B. aegyptiaca have been a valuable source of natural active constituents of products that maintain human health and in the treatment of many human diseases (Table 1). It is widely used in African (Sudan, Ethiopia, Nigeria, Senegal, Chad, Egypt) and Asian countries. Flavonoids is a major constitute of tree bark, root and stem and it exhibited in vitro antioxidant potential (Rice-Evans et al., 1996). Further, furanocoumarins which have been isolated from the various parts showed several biological activities such as anti-inflammatory, antioxidant, anti-neoplastic as well as bone health preservation both *in vitro* and *in vivo*. Further, furanocoumarins wielded antiproliferative activities against cancer cell growth through several molecular pathway modulation, such as regulation of the signal transducer and activator of phosphatidylinositol-3-kinase/AKT, nuclear factor-kB, and mitogen-activated protein kinase expression (Hung et al., 2016). 5-Methoxypsoralen, also known as bergapten, is a linear furanocoumarin that occurs naturally and has been used to control vitiligo and psoriasis (Seida et al., 1981; McNeely & Goa, 1998).

Saponins are triterpenoid glycosides or steroid that has hypocholesterolaemic, anticarcinogenic and immunostimulant properties (Francis et al., 2007). A significantly high inhibitory activity against hyperglycemia was expressed only from the furostanol saponin as it successfully inhibited α-glucosidase and aldose reductase, showing that these α-glucosidase (AG) inhibitors are responsible for reversibly delaying the absorption of glucose from the gastrointestinal tract (Campbell et al., 1996; Yabe-Nishimura, 1998; Saharan et al., 2008; Abdel Motaal et al., 2015). Similarly, anti-hyperglycemic properties of *B. aegyptiaca* fruit have been reported by Farag et al. (2015), these researchers reported that this antihyperglycemic properties may be because of the presence of trigonelline; a pyridine containing alkaloids. Trigonelline acts by affecting cell regeneration, insulin secretion, enzymes affecting glucose metabolism, and diminishes the oxidative stress in type 2 diabetes (Amaro et al., 2014).

The extracted oil from *B. aegyptiaca* inhibited human cancer cell line growth and had anticancer activity against brain, liver and lung carcinoma cell lines (Al Ashaal et al., 2010; Chothani &

Table 1 Therapeutic use of various plant parts of *B. Aegyptiaca* against various diseases

Plant Part	Cured Diseases	References
Complete Plant	Jaundice, anthelmintic, rheumatism, CNS depressant, fungicidal, larvicidal, molluscicidal, insecticidal properties, it also used to remove intestinal parasites	Neuwinger, 1996; Mohamed et al., 1999, Koko et al., 2000; Koko et al., 2005; Wiesman & Chapagain, 2006; Chapagain et al., 2009; Patil et al., 2010; Abdulmalik et al., 2011; Shalaby et al., 2012
Stem/Root Bark	Yellow fever, jaundice, antiangiogenic, antitumor, antioxidant, antimalarial, anti trypanocidal activity, cytotoxicity, mental diseases, diarrhea, epilepsy, treatment of Syphilis round worm infection, haemorrhoid, fish poison, antivinom against viper venom and syphilis	Bukar et al., 2004; Katewa et al., 2004; Wurochekke & Nok, 2004; Koch et al., 2005; Gad et al., 2006; Ojo et al., 2006; Wufem et al., 2007; Ahmad Hassan et al., 2016
Fruit	Skin diseases, sleeping sickness, oral hypoglycemia, cytotoxicity, antitumor effects, antioxidant, antifertility, insecticidal activity, anticonvulsant effect, cure mouth ulcer, boils and burns, whooping cough, effective antischistosomal remedy, act as an antidote to arrow poison	Rao et al., 1997; Wiesman & Chapagain, 2003; Katewa et al., 2004; Koch et al., 2005; Koko et al., 2005; Gad et al., 2006; Ojo et al., 2006; Gnoula et al., 2008; Thirupathi et al., 2009; Al-Ghannam et al., 2013; Molla et al., 2013; Wabale, 2017
Seed	Antitumor, anti-cancer antibacterial, antioxidant, antimalarial activity, effective antischistosomal remedy and cure cough, colic pain	Wiesman & Chapagain, 2003; Bukar et al., 2004; Koko et al., 2005; Ojo et al., 2006; Gnoula et al., 2008; Kusch et al., 2011; Mostafa et al., 2016
Seed oil	Skin diseases, diabetes, hypoglycemia, sleeping sickness and promising for HIV/AIDS patients	Cook et al., 1998; Sheded et al., 2006; Alashaal et al., 2010
Leaves	Wound healing, curing anthrax, antihelminthic activities, to clean malignant wounds	Ojo et al., 2006; Kommu et al., 2013
Root	Stomach pain, anthrax, and the infusion of root also acts as an antidote to snake bite	Ojo et al., 2006

Vaghasiya, 2011). Presence of the B-sitosterols has been reported from the *B. aegyptiaca* extract, Wilt et al. (1999) reported anti-inflammatory effects of this metabolite. Also, the presence of phytosterol, especially β-sitosterol articulated antioxidant and antineoplastic activity (Al Ashaal et al., 2010). The antimicrobial effects with stearic, oleic and linoleic acids in addition to β-sitosterol revealed with greatest inhibition against *Candida albicans* and *Staphyloccous aureus* when extract efficacy was compared with Tavanic and Nystatine as standards (Al Ashaal et al., 2010; Chothani & Vaghasiya, 2011).

Further, Chaudhry & Khoo (2004) reported antiviral activity of *B. aegyptiaca* plant against HIV/AIDS. Similarly, virucidal activity of *B. aegyptiaca* oil against Herpes simplex virus type 1 (HSV1) has been reported by Al Ashaal et al. (2010).

The fixed oil of *B. aegyptiaca* possesses anthelmintic activity against *Schistosoma mansoni* and *Fasciola gigantica*, it found equal effective to praziquantel which used as a positive control (Al Ashaal et al., 2010). Dose-dependent effect of *B. aegyptiaca* oil on micronuclei and chromosomal aberrations was also reported by Al Ashaal et al. (2010).

The methanolic and ethanolic extract of *B. aegyptiaca* leaves have diuretic effect when tested on Wistar albino rats against Frusemide as a standard (Wani et al., 2010). The methanolic extract of *B. aegyptiaca* fruits also proved as a cheap alternative of more expensive anthelmintics as it showed a potent and progressive effect on the cuticle of adult *Toxocara vitulorum* and an inhibitory effect on *T. vitulorum* egg development (Shalaby et al., 2012).

5 Toxicology of Phytochemicals

Discussions of the phytochemical and ethanopharmaceutical properties of *B. aegyptiaca* have established that this is a values plant for the traditional and modern medicine. Though drug obtained from plant have limited chances of side but sometime improper dose can cause adverse effect of humans. Therefore toxicological study of various phytochemicals is must, Mariam et al. (2013) studied the toxicological effect of *B. aegyptiaca*, and

revealed that oral administration of the extract at the specified doses showed any toxicity on liver cells. Suky et al. (2011) studied acute toxicity of 200-2000 mg/kg ethanol extract of *B. aegyptiaca* and observed that extract did not have any behavioural changes or mortality even at a dose of 2000 mg/kg which indicate the safety of this extract. Similarly, Obidah et al. (2009) also studied the toxicological aspect of crude seed oil and suggested that crude oil did not result in marked changes in the toxicological parameters of experimental animal, which suggested that crude oil is edible and consumption of the crude oil at the present level of exposure may be of no serious safety concern, especially on liver and kidney injury. Findings of Absalom et al. (2013) are contradictory to the findings of previous two, these researchers investigate the toxic effects of *B. aegyptiaca* fruit extract on the mortality and behaviour of juveniles of African catfish (*Clarias gariepinus*) and reported that at higher concentration (64.0gL-1) fruit extract caused fish mortality, and its toxic effects lowered the values of some haematological parameters compared to the control group.

Conclusions

This review confirms the potential of *B. aegyptiaca* as traditional medicine and also established its antidiabetic, antiviral, antibiotic, anticancer, antihelminthic and molluscicidal activities . Presence of the flavonoids, terpenoids, steroids, alkaloids and saponins as an bioactive entities was also confirmed by this review article. Considerable outstanding activities of *B. aegyptiaca*, suggested by this review article generate the opportunity to precede detailed study on the mechanism of actions of these compounds with respect to feature aspects of molecular investigations.

Conflict of interest

All the authors declare that there is no conflict of interest.

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