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REVIEW ARTICLE
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Hingot (*Balanites aegyptiaca*): Mechanistic Pharmacology, Phytochemistry, and Recent Therapeutic Advances

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ABSTRACT

Balanites aegyptiaca **(L.) Delile (Hingot, Ingudi) is a xerophytic tree of the family Zygophyllaceae distributed across arid zones of Africa, the Middle East, and South Asia, with documented use in Ayurveda and African folk medicine for hepatic disorders, parasitic infections, and diabetes. This review integrates phytochemistry, mechanistic pharmacology, computational analyses, and nanoformulation research published through early 2026. More than 84 physiologically active compounds have been identified, including furostanol saponins (balanitins 1-7), diosgenin, phenolic acids, flavonoids, and trigonelline. Antidiabetic activity is the most extensively studied property, mediated through α-amylase and α-glucosidase inhibition, PPARγ–GLUT4 modulation, and network pharmacology targets including IL-6, PPARα, GCK, and GCG. Preclinical evidence supports additional anticancer, antimicrobial, anti-inflammatory, and hepatoprotective activities. Molecular docking identifies balanitesin as a high-affinity α-amylase inhibitor with binding stability confirmed by molecular dynamics simulation. Chitosan and silver nanoparticle formulations have demonstrated improved antidiabetic and anticancer outcomes over crude extracts in preclinical models.**

One pilot randomised controlled trial in type 2 diabetes showed significant glycaemic improvement without adverse effects. Large-scale clinical trials, standardised extracts, and human pharmacokinetic data remain absent, representing the primary barriers to therapeutic translation.

Keywords: Balanites aegyptiaca; furostanol saponins; network pharmacology; molecular docking; nanoformulations; antidiabetic activity.

INTRODUCTION

Balanites aegyptiaca (L.) Delile belongs to the family Zygophyllaceae and grows as a spiny, multi-branched tree reaching approximately 10 m in height [Gautam et al., 2023]. It is a xerophyte, adapted to sandy and alluvial soils under conditions of low rainfall and high ambient temperature across the dryland belt spanning sub-Saharan Africa, the Arabian Peninsula, and the Indian subcontinent [Murthy et al., 2020, Al-Thobaiti and Zeid, 2018]. In India, the species occurs predominantly in arid Rajasthan, where it is commonly called 'Hingot', and is documented in Ayurvedic literature under the synonym 'Ingudi' in classical texts including the Bhavaprakasha Nighantu [Chothani and Vaghasiya, 2011]. The plant's tolerance to drought and marginal soils has sustained its role in subsistence medicine across these regions for centuries [Shinde et al., 2025].

Traditional therapeutic applications span multiple systems of medicine. Ayurvedic practitioners have used various parts of the plant for jaundice, worm infestations, skin diseases, haemorrhoids, and hepatic and splenic disorders [Sharma and Sharma, 2026]. In African and Middle Eastern ethnomedicine, documented uses include malaria, sleeping sickness, wound management, and sexually transmitted infections, with the fruit, bark, root, and seed kernel each serving distinct therapeutic roles [Zein et al., 2024, Hamad et al., 2024]. Across these traditions, the breadth of indications reflects the diverse phytochemical composition of the species rather than activity confined to a single compound class.

Chemical investigations have identified over 80 physiologically active compounds from different plant parts [Shinde et al., 2025]. These include furostanol and spirostanol saponins such as balanitin-1 through balanitin-7, flavonoid glycosides, phenolic acids, alkaloids including trigonelline, pregnane glycosides, and steroidal aglycones of which diosgenin has received the most pharmacological attention [Shinde et al., 2025]. Saponin content is particularly concentrated in the fruit and seed kernel [Shinde et al., 2025]. The distribution of these compounds varies by organ and, likely, by geographic accession, though comparative metabolomic studies across Indian and African populations remain absent from the literature.

Published reviews through 2023 documented traditional uses, broad phytochemical inventories, and preliminary pharmacological data but did not address molecular mechanisms at the receptor or pathway level, nor did they cover in silico target identification or nanomedicine-based delivery strategies [Dey, 2023]. Work published from 2024 onwards has begun to fill these gaps. Network pharmacology combined with GC-MS profiling has mapped probable antidiabetic targets including IL-6, PPARα, GCK, and GCG [Gautam et al., 2025]. Chitosan nanoparticles loaded with B. aegyptiaca extract produced significantly improved glycaemic outcomes in streptozotocin-induced diabetic rats compared to the crude extract [Alahmer et al., 2024], and silver nanoparticles prepared from seed extract showed

antidiabetic activity across muscle and pancreatic cell lines [Bhardwaj et al., 2024]. A systematic review of 2025 assessed preclinical antidiabetic evidence using SYRCLE risk-of-bias criteria, providing the first structured appraisal of study quality in this literature [Odeniran et al., 2025].

This review integrates phytochemistry, mechanistic pharmacology, computational studies, and nanoformulation research on B. aegyptiaca published up to early 2026, with particular focus on molecular-level evidence and drug delivery advances that prior reviews did not address.

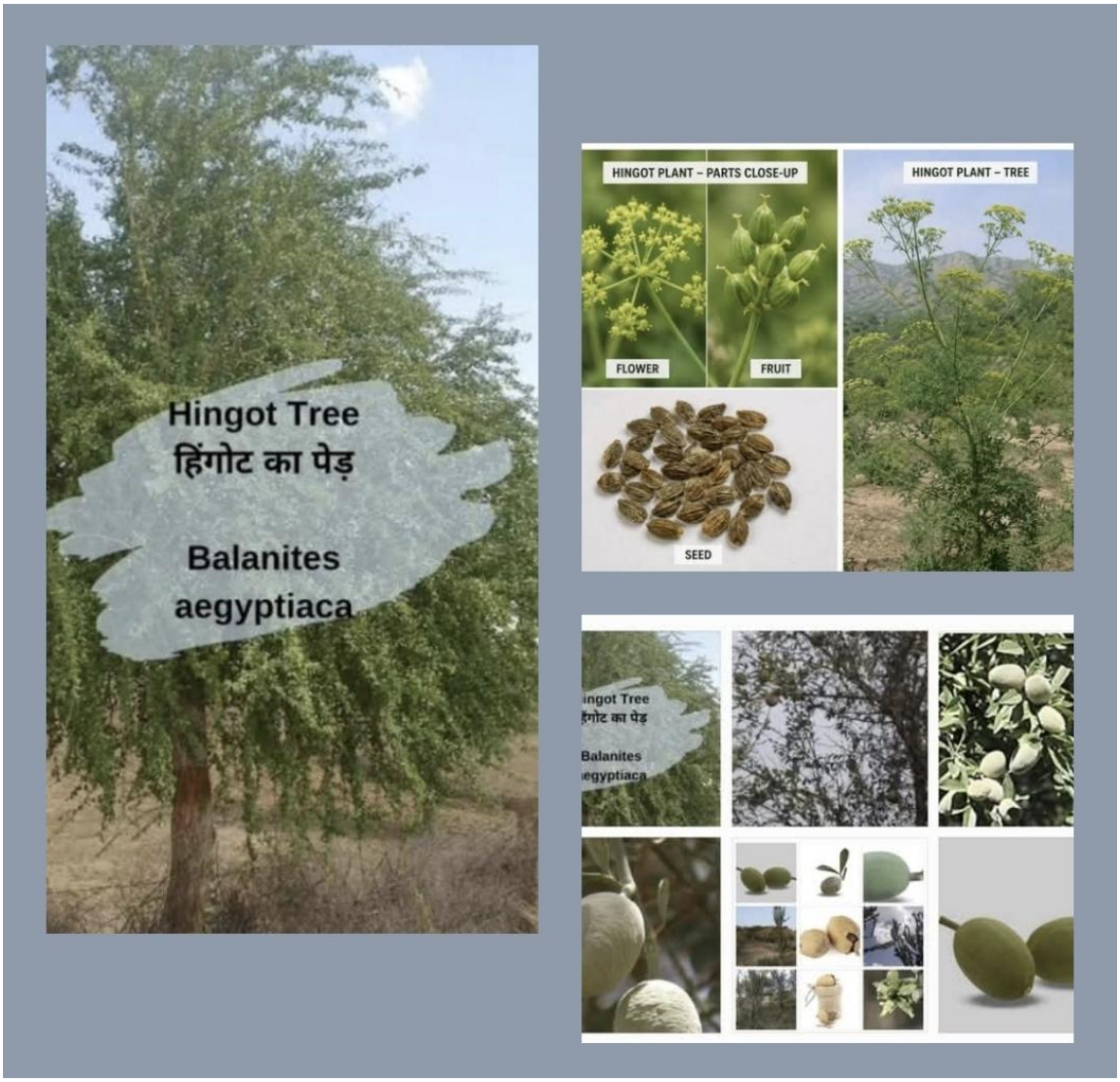

Figure 1. Macromorphological characteristics of *Balanites aegyptiaca* including floral structures, developing fruits, seed morphology, and vegetative architecture.

Botanical Profile, Ethnopharmacology & Phytochemistry

Botanical Description and Morphology

Balanites aegyptiaca is a spinous, multi-branched woody tree reaching approximately 10 m, distributed across arid and semi-arid zones of sub-Saharan Africa, the Middle East, and the Indian subcontinent [Ahmad and Mariod, 2019].

Fruits develop as fleshy drupes, green when immature and ripening to a smooth, yellowish mesocarp with edible, bittersweet pulp [1,20]. The hard pyrene encloses an oil-rich kernel containing 30 to 60% fixed oil alongside appreciable protein content [Ahmed et al., 2019]. Morphological parameters, including fruit length, diameter, pulp-to-seed ratio, and kernel dimensions, show marked tree-to-tree variation within populations studied in Burkina Faso and Sudan, and this variability correlates with oil yield, fatty acid composition, and antioxidant capacity [Ahmed et al., 2019]. Polyphenol content, tannin levels, and radical-scavenging activity also differ substantially across individual trees and collection sites within Mauritania [Abdelaziz et al., 2020]. Provenance-dependent variation in leaf and fruit metabolite profiles is documented across accessions from Egypt, Sudan, Saudi Arabia, and Yemen [Khamis et al., 2020], but no chemotypic comparison between Indian and African accessions using standardized metabolomic pipelines has been published to date.

Ethnopharmacological Uses

B. aegyptiaca is used medicinally across South Asia and Africa, with documented applications spanning nearly every plant organ. In classical Ayurvedic texts and Indian folk practice, preparations from the fruit, bark, seed, and root have been recorded for jaundice, syphilis, yellow fever, liver and spleen disorders, leprosy, worm infestations, skin diseases, constipation, diarrhea, hemorrhoids, and dysentery [Yadav and Panghal, 2010]. In Rajasthan, the plant is cited specifically for intestinal parasites, wounds, epilepsy, asthma, malaria, and fever [Tesfaye, 2015].

Table 1. Ethnomedicinal uses of *Balanites aegyptiaca* by geographic tradition and plant part.

Region/ Tradition	Plant Part(s)	Reported Uses
Rajasthan/Indian folk	Fruit, root, leaf, bark	Jaundice, intestinal worms, wounds, malaria, syphilis, epilepsy, asthma, fever, constipation, diarrhoea, haemorrhoids
Ayurveda (classical)	Fruit, seeds, bark, roots	Jaundice, syphilis, yellow fever, liver and spleen disorders, metabolic disorders, leprosy, skin diseases, whooping cough, diarrhoeal states
Sahel/Sahara (Africa)	Fruit pulp	Diabetes, hypertension, purgative, antiparasitic, schistosomicide
Sahel/Sahara (Africa)	Kernel oil	Topical application for paronychia and dermal infections
Wider African use	Leaves, roots, stem, fruit	Malaria, helminth infections, sore throat, eye discomfort, liver disease, fish poison, mild sedative

Across the Sahel and Sahara, fruit pulp is the most widely utilized part. A survey conducted in Mauritania found that 97% of informants reported fruit pulp as a treatment for diabetes and hypertension, while kernel oil is applied topically for paronychia and dermal infections.

In wider African use, leaf, root, and stem preparations are documented for malaria, helminth infections, sore throat, eye discomfort, and liver disease, and the plant has also been recorded as a fish poison and mild sedative in certain communities [Farag et al., 2023]. The convergence of antidiabetic, anti-infective, hepatoprotective, and purgative indications across geographically distant traditions aligns with activities subsequently confirmed in preclinical studies [Abdelaziz et al., 2020].

Phytochemistry

More than 80 physiologically active compounds have been identified from B. aegyptiaca across the fruit pulp, seed kernel, leaves, bark, and roots [Shinde et al., 2025]. Analytical approaches, including GC-MS, UHPLC-ESI-QTOF-MS/MS, LC-MS, NMR-based metabolomics, and molecular networking, have substantially expanded the known inventory beyond what earlier spectrophotometric screening methods could resolve [Wakawa et al., 2018].

Saponins and sapogenins. Furostanol and spirostanol steroidal saponins represent the dominant and most pharmacologically studied compound class. Balanitins 1 through 7 and balanitoside are concentrated primarily in the fruit pulp and seed kernel, where saponin content reaches approximately 7% of dry mass in each fraction [Abdelaziz et al., 2020]. MALDI-TOF- and UPLC-MS-based profiling has resolved at least 24 distinct furostanol saponins from fruit mesocarp, kernels, and roots, with molecular architectures incorporating 2 to 8 sugar units [Khamis et al., 2020]. The steroidal aglycones diosgenin and yamogenin are found in fruits, roots, and seeds and serve industrially as starting materials for the synthesis of cortisone and oral contraceptives [Tesfaye, 2015].

Phenolic acids and phenolics. Fruit pulp contains approximately 260 mg gallic acid equivalents per 100 g dry mass of total polyphenols alongside soluble tannins. At least 14 phenolic compounds have been catalogued across plant parts, with gallic acid and chlorogenic acid detected consistently in LC-MS and GC-MS surveys of fruit and leaf fractions. Quantitative analysis of aqueous fruit extract reports a phenol content of approximately 227 mg per 100 g. Total phenolic content and antioxidant capacity both show provenance-dependent variation across African collection sites [Khamis et al., 2020].

Flavonoids. At least 14 flavonoids have been documented across plant parts. Rutin, quercetin, isorhamnetin, rutin-3-glycoside, and 3,7-diglycosides are identified by UPLC-MS/MS and NMR-based metabolomics in fruits, stems, and leaves. Isorhamnetin concentration increases with fruit maturation and has been proposed as a chemical marker of ripeness. Aqueous fruit extract contains approximately 288 mg flavonoids per 100 g dry mass.

Alkaloids. Alkaloids are consistently detected in fruits, seeds, leaves, and roots, though their presence in stem bark appears chemotype-dependent [Rickson et al., 2025]. Trigonelline is identified by NMR and UPLC-MS in both immature and mature fruit, with concentrations highest in unripe material. Nicotinic acid and additional nitrogen-containing metabolites are detected in broader metabolomic surveys of different plant parts.

Steroids and fixed oils. Eight steroidal compounds and pregnane glycosides are distributed across seeds, fruits, and vegetative tissues. Seed kernels contain 30 to 60% fixed oil, with unsaturated fatty acids representing approximately 74% of total lipid content. Oleic and linoleic acids predominate, while palmitic, linolenic, and stearic acids are quantified by GC-MS of fatty acid methyl esters, with proportions varying by fruit morphotype and geographic provenance.

Modern profiling and chemotypic gaps. Multiplex metabolomics integrating NMR, UPLC-MS/MS, and GC-MS with molecular networking has simultaneously annotated saponins, phenolics, flavonoids, alkaloids, sugars, amino acids, and fatty acids across leaves, stems, seeds, and fruits. Provenance studies across accessions from Egypt, Sudan, Saudi Arabia, and Yemen demonstrate that metabolite levels and associated bioactivities differ considerably by geographic origin. No equivalent comparison between Indian accessions, particularly from Rajasthan, and African populations using standardised analytical pipelines has been published, and this remains a substantive gap in the literature.

Table 2. Major phytochemical classes of *Balanites aegyptiaca*, principal plant parts, representative compounds, and analytical approaches used for their characterization.

Compound Class	Representative Compounds	Principal Plant Part(s)	Analytical/Isolation Approach
Steroidal saponins & sapogenins	Balanitin-1 through -7, balanitoside, diosgenin, yamogenin	Fruit pulp, seed kernel, roots	Solvent extraction; MALDI-TOF/MS; UPLC-MS/MS; LC-MS; column chromatography
Phenolic acids & tannins	Gallic acid, chlorogenic acid, soluble tannins	Fruit pulp, leaves, stems, kernel	Folin-Ciocalteu spectrophotometry; HPLC; LC-MS; GC-MS
Flavonoids	Rutin, quercetin, isorhamnetin, rutin-3-glycoside, 3,7-diglycosides	Fruits, leaves, stems	UPLC-MS/MS; NMR-based metabolomics; colorimetric assays
Alkaloids	Trigonelline, nicotinic acid	Immature and ripe fruits, leaves, seeds	NMR; UHPLC-ESI-QTOF-MS/MS; GC-MS
Steroids & pregnane glycosides	8 steroidal compounds, pregnane glycosides	Seeds, fruits, vegetative tissues	Phytochemical screening; FTIR; GC-MS; LC-MS
Fixed oils & fatty acids	Oleic acid, linoleic acid, palmitic acid, linolenic acid	Seed kernel, fruit mesocarp	Soxhlet extraction; GC-MS of fatty acid methyl esters; LC-MS

Mechanistic Pharmacology

Antidiabetic Activity

Enzyme inhibition. Polysaccharides isolated from *B. aegyptiaca* fruits inhibited α-amylase and α-glucosidase in vitro, with IC_{50} values of approximately 44 and 27 mg/mL respectively, demonstrating capacity to slow postprandial glucose absorption through direct enzyme inhibition [Anon, 2024]. Methanolic extracts achieved α-amylase inhibition comparable to acarbose in network pharmacology-guided in vitro assays, further confirming this enzyme as a primary pharmacological target. In silico docking of leaf phenolic compounds against both enzyme binding sites showed that 2-methoxy-4-(1-propenyl)-phenol produced binding

energies similar to acarbose across α-amylase and α-glucosidase simultaneously [Mhya et al., 2021]. A separate computational study identified balanitesin and the compound SN0224203 as high-affinity α-amylase ligands with docking scores exceeding the reference inhibitor, and binding stability was confirmed across 50 to 300 ns molecular dynamics simulations [Gautam et al., 2026]. The convergence of these in vitro and in silico findings establishes carbohydrate enzyme inhibition as the most consistently demonstrated antidiabetic mechanism for this plant.

Insulin signalling *and metabolic effects.* In NA/STZ-induced type 2 diabetic rats, aqueous fruit and seed extracts reduced hyperglycaemia and dyslipidaemia, restored hepatic glycogen content, and normalised glucose-6-phosphatase and glycogen phosphorylase activities. Concurrent reductions in hepatic lipid peroxidation and increases in glutathione, SOD, GPx, and GST activity indicate that glycaemic improvement is coupled to antioxidant defence rather than being an isolated enzymatic effect. Steroidal saponins of the diosgenyl-type furostanol class, particularly the balanitins, are identified as primary insulinotropic and insulin-sensitising candidates in systematic appraisals of the preclinical literature, consistent with earlier reports of α-glucosidase and aldose reductase inhibition by this compound class. A randomised double-blind pilot clinical trial further demonstrated significant reductions in blood glucose and lipid markers in type 2 diabetic patients receiving standardised fruit extract capsules, without reported adverse effects, providing the only human-level evidence currently available for antidiabetic efficacy.

Network pharmacology targets. GC-MS-driven network pharmacology mapping of *B. aegyptiaca* phytoconstituents identified IL-6, PPARα, GCG, and GCK as central diabetes-relevant targets, with pathway enrichment concentrated in insulin signalling and glucose homeostasis [16]. A focused α-amylase-centred network analysis linked SN0224203 to GCK, AKT3, PIK3CA, PIK3R1, PTPN1, and mTOR within type 2 diabetes and insulin resistance pathway clusters [32]. These in silico target maps support a multi-target antidiabetic profile that spans inhibition of carbohydrate-digesting enzymes at the intestinal level, modulation of the inflammatory mediator IL-6, regulation of lipid and glucose metabolism through PPARα and GCK, and indirect effects on pancreatic glucagon signaling through GCG [Gautam et al., 2026].

Anticancer Activity

Cytotoxicity across cell lines. Methanolic fruit extract produced concentration-dependent cytotoxicity against MCF-7 (breast), PC-3 (prostate), and Caco-2 (colorectal) cancer cell lines, with IC_{50} values of approximately 112, 92, and 87 µg/mL, respectively [Ibrahim et al., 2022]. Selectivity was indicated by substantially lower toxicity toward normal Vero cells (IC_{50} approximately 570 µg/mL), yielding selectivity indices between 5 and 6.5 [Ibrahim et al., 2022]. Phytoconstituent fractions from *B. aegyptiaca* combined with those of *Pterocarpus marsupium* showed IC_{50} values of approximately 40 to 45 µg/mL against HepG2 and U87MG cell lines [Vashishth and Kataria, 2025, Vashishth et al., 2025]. Maturity-dependent differences in cytotoxicity were documented in a metabolomic study where immature fruit extracts produced stronger HepG2 inhibition than mature fruit extracts (IC_{50} 118 vs 270 µg/mL), a difference that corresponded to distinct metabolite profiles between ripening stages [Abdelsalam et al., 2025].

At the isolated compound level, balanitin-6 and balanitin-7, diosgenyl furostanol saponins purified from *B. aegyptiaca*, displayed sub-micromolar IC_{50} values against PC-3 and LoVo cell lines, exceeded the antiproliferative potency of etoposide and oxaliplatin in direct comparisons, and increased survival in a murine leukaemia model [Gnoula et al., 2008].

Apoptotic mechanism. In PC-3 cells, methanolic fruit extract induced G_0/G_1 arrest and raised total apoptosis from approximately 0.6% in untreated controls to 19%, with concurrent upregulation of BAX and p53 and downregulation of BCL2. Comparable apoptotic profiles were recorded in HepG2 and U87MG cells treated with active fractions, where p53 and Bax upregulation accompanied BCL2 downregulation. Metabolomic docking analysis of immature fruit identified theophylline as a constituent with high affinity for the BCL-2 binding pocket, supporting a direct compound-level interaction with this anti-apoptotic protein. Furostanol saponin-coated silver nanoparticles enhanced antiproliferative activity against HepG2 and Caco-2 cells and modulated apoptosis-related gene expression more substantially than crude extract alone [Yassin et al., 2017]. Collectively, the data point to intrinsic mitochondrial apoptosis mediated through the Bax/Bcl-2 axis with p53 involvement, with downstream caspase-3/9 activation as a probable mechanistic step pending direct measurement.

Cell cycle and emerging targets. G_1-phase arrest is consistently documented across cell line studies using fruit extract. Balanitin-6 and balanitin-7 independently caused actin disorganisation and ATP depletion in cancer cells, impairing proliferation and migration through mechanisms distinct from membrane disruption [Yassin et al., 2017]. Network pharmacology links BA phytochemicals to PI3K/AKT/mTOR pathway components, placing cyclin-CDK complexes, including CDK4, as plausible downstream targets that have not yet been directly measured in *B. aegyptiaca* studies.

Antimicrobial and Antiparasitic Activity

Antibacterial activity. Hydroethanolic bark extract inhibited multidrug-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* isolated from clinical wound samples at MIC values of 2.5 to 12.5 µg/mL and 12.5 µg/mL, respectively, with MBC values between 2.5 and 50 µg/mL [Anani et al., 2015]. Methanolic fruit extract showed activity against *S. aureus*, *Klebsiella pneumoniae*, and *E. coli* at a uniform MIC of 62.5 µg/mL. Seed oil inhibited *S. aureus*, *E. coli*, *Bacillus subtilis*, and *P. aeruginosa*, consistent with the antimicrobial contribution of its high unsaturated fatty acid content [Ibrahim and Wady, 2021]. Stem bark extract showed antifungal activity against *Candida albicans* at an MIC of 125 µg/mL in an ethnopharmacological screen of Tanzanian medicinal plants [Maregesi et al., 2008].

Antiparasitic activity. In goats experimentally infected with *Haemonchus contortus*, ethanol fruit extract reversed infection-induced elevation of MDA, IL-3, IL-6, IL-10, TNF-α, and Bax and restored GSH, SOD, and GST levels in abomasal tissue, with antioxidant effects that exceeded those of albendazole under the same conditions [Sedky et al., 2024]. This profile indicates tissue-protective action through oxidative stress reduction and cytokine downmodulation as a component of antiparasitic efficacy. Antiplasmodial, antileishmanial, and antischistosomal activities are documented in pharmacological reviews, though quantitative IC_{50} data and defined molecular targets for these activities are incompletely characterised in the primary experimental literature.

Table 3. Selected preclinical pharmacological studies of *Balanites aegyptiaca* showing experimental model, extract or fraction used, principal outcomes, and mechanistic highlights.

Activity	Experimental Model	Extract/Fraction	Principal Outcome	Mechanistic Highlights
Antidiabetic	NA/STZ-induced diabetic rats	Aqueous fruit and seed extracts	Reduced hyperglycaemia and dyslipidaemia; restored hepatic glycogen	Normalized glucose-6-phosphatase and glycogen phosphorylase; increased GSH, SOD, GPx, GST
Antidiabetic	In vitro enzyme assay	Fruit polysaccharides	α-amylase $IC_{50} \approx 44$ mg/mL; α-glucosidase $IC_{50} \approx 27$ mg/mL	Direct carbohydrate enzyme inhibition
Antidiabetic	STZ-induced diabetic rats	Chitosan NPs loaded with BA extract	Greater reduction in fasting blood glucose and triglycerides than free extract	Controlled release; enhanced bioavailability; pancreatic β-cell neogenesis
Antidiabetic	Randomized double-blind pilot trial (n=30, Type 2 diabetes)	Standardized pericarp extract capsules	Significant reduction in blood glucose and lipid markers; no adverse effects	Not mechanistically detailed in trial report
Anticancer	MCF-7, PC-3, Caco-2 cell lines	Methanolic fruit extract	IC_{50} 112, 92, 87 µg/mL respectively; selectivity index 5–6.5 vs Vero cells	G_0/G_1 arrest; BAX and p53 upregulation; BCL2 downregulation
Anticancer	HepG2, U87MG cell lines	Methanolic extract fractions	IC_{50} approximately 40–45 µg/mL	p53 and Bax upregulation; BCL2 downregulation
Anticancer	HepG2 cells	Immature vs mature fruit extract	IC_{50} 118 µg/mL (immature) vs 270 µg/mL (mature)	Maturity-dependent metabolomic differences; BCL-2 binding by theophylline

Anticancer	**PC-3, LoVo cell lines; murine leukaemia model**	**Isolated balanitin-6 and balanitin-7**	**Sub-micromolar IC_{50}; exceeded etoposide and oxaliplatin potency; increased murine survival**	**Actin disorganization; ATP depletion; impaired migration**
Anticancer	HepG2, Caco-2 cell lines	Saponin-coated AgNPs	83–85% growth inhibition at nontoxic doses	Enhanced apoptotic gene modulation vs crude extract
Antibacterial	MDR wound isolates (*S. aureus*, *P. aeruginosa*)	Hydroethanolic bark extract	MIC 2.5–12.5 µg/mL (*S. aureus*); 12.5 µg/mL (*P. aeruginosa*)	Phenolic-associated membrane disruption
Antibacterial	*S. aureus*, *K. pneumoniae*, *E. coli*	Methanolic fruit extract	Uniform MIC 62.5 µg/mL	Not mechanistically detailed
Antibacterial	*S. aureus*, *E. coli*, *B. subtilis*, *P. aeruginosa*	Seed oil	Growth inhibition across all strains	Attributed to high unsaturated fatty acid content
Antifungal	*Candida albicans*	Stem bark extract	MIC 125 µg/mL	Not mechanistically detailed
Antiparasitic	*H. contortus*-infected goats	Ethanol fruit extract	Reversed infection-induced oxidative and cytokine changes; antioxidant effect exceeded albendazole	Reduced MDA, IL-3, IL-6, IL-10, TNF-α; restored GSH, SOD, GST; modulated Bax/Bcl-2
Anti-inflammatory	Turpentine-induced inflammation in rats	Aqueous-acetone gall and leaf extract	Reduced leukocyte counts, serum nitrites/nitrates, and total oxidative status; increased total antioxidant response	Systemic antioxidant and anti-inflammatory effects
Anti-inflammatory	Egg albumin denaturation model	n-Hexane extract	Inhibition exceeded aspirin	COX-2/iNOS pathway modulation proposed
Antioxidant	DPPH, ABTS, FRAP, hydroxyl radical assays	Fruit polysaccharides; n-hexane and ethyl acetate fractions	Comparable to ascorbic acid; 68% protein denaturation inhibition at 0.5 mg/mL	Free radical scavenging; ferric reducing power

Figure 2: Mechanistic Pharmacological Pathways.

Anti-inflammatory, Antioxidant, Hepatoprotective, and Other Activities

Anti-inflammatory and antioxidant. Fruit polysaccharides showed activity across DPPH, ABTS, hydroxyl radical scavenging, ferric-reducing power, and total antioxidant capacity assays, alongside approximately 68% inhibition of protein denaturation at 0.5 mg/mL, indicative of anti-inflammatory potential. Among solvent fractions, n-hexane and ethyl acetate extracts showed antioxidant capacity comparable to ascorbic acid, and the n-hexane fraction exceeded aspirin in inhibition of egg albumin denaturation in a standard anti-inflammatory model. In vivo, aqueous-acetone extracts of *B. aegyptiaca* galls and leaves significantly reduced leukocyte counts, serum nitrites and nitrates, and total oxidative status while increasing total antioxidant response in turpentine-induced inflammation in rats [Meda et al., 2020].

Hepatoprotective activity. In NA/STZ diabetic rats, aqueous fruit and seed extracts reduced hepatic lipid peroxidation, restored glutathione and antioxidant enzyme activities, and normalised glucose-6-phosphatase and glycogen phosphorylase levels. The mechanistic pattern of reduced oxidative stress paired with enhanced endogenous antioxidant enzyme activity is consistent with NF-κB suppression and Nrf2/HO-1 pathway activation, as proposed in recent comprehensive reviews of the plant's pharmacology.

Other activities. Reviews document nephroprotective, wound-healing, neuroprotective, and antifertility activities attributed to the saponin fraction and broader phytochemical inventory.

Neuroprotective effects include acetylcholinesterase inhibition relevant to Alzheimer's disease models, and antifertility data describe spermicidal activity of saponin-rich fractions. Systematic mechanistic endpoints for these activities, including direct COX-2 and iNOS measurements and AChE kinetic parameters, have not been reported in primary experimental studies and represent open areas for targeted investigation.

Table 4. Representative molecular docking results for *Balanites aegyptiaca*-derived compounds against pharmacologically relevant protein targets.

Ligand	Target Protein	Docking Score (kcal/mol)	Binding Free Energy ΔG (kcal/mol)	Key Interacting Residues	Notes
Balanitesin	Human pancreatic α-amylase	−14.406	−125.47	Not specified	Outperformed acarbose-derived reference; top BA hit
SN0224203	Human pancreatic α-amylase	−13.1	−128.41	His201, Glu240, His305	Stable across 50–300 ns MD simulation
Acarbose-derived standard	Human pancreatic α-amylase	−12.500	−81.275	Not specified	Reference inhibitor for comparison
2-Methoxy-4-(1-propenyl)-phenol	α-Amylase and α-glucosidase	−4.4 / −4.2	Not reported	Not specified	Lipinski-compliant; comparable to acarbose on one site
Precose	SARS-CoV-2 Mpro	−9.0	Not reported	His41, Glu166, Asp189	MD-confirmed stable binding; antiviral repurposing potential

Computational Studies & Nanoformulations

Network Pharmacology & Molecular Docking

GC-MS-guided network pharmacology has been applied to map *B. aegyptiaca* phytoconstituents to antidiabetic molecular targets. One study integrated GC-MS phytochemical profiling with Cytoscape-based target network construction and STRING protein interaction analysis, identifying IL-6, PPARα, GCG, and GCK as central nodes within insulin signalling and glucose homeostasis pathways that are modulated by BA-derived compounds. In vitro validation in the same work demonstrated that the methanolic extract achieved α-amylase inhibition comparable to acarbose, consistent with the computational target predictions. A dedicated molecular docking study on human pancreatic α-amylase identified balanitesin as the top-performing BA compound, with a docking score of −14.406 kcal/mol and binding free energy of −125.47 kcal/mol, both exceeding the acarbose-derived reference standard (docking score −12.500 kcal/mol; ΔG −81.275 kcal/mol).

A structurally analogous compound identified through similarity-based library expansion, SN0224203, produced a docking score of approximately −13.1 kcal/mol and ΔG of −128.41 kcal/mol, forming stable hydrogen bonds with catalytic residues His201, Glu240, and His305 throughout 50 to 300 ns molecular dynamics simulations. In silico ADME/T profiling of both compounds indicated oral suitability, acceptable aqueous solubility, and favourable safety indices, alongside low central nervous system penetration.

Independent in silico work on BA leaf phenolic compounds reported Lipinski-compliant drug-likeness for multiple constituents, with docking energies of approximately −4.4 and −4.2 kcal/mol against α-amylase and α-glucosidase, respectively. ADMET predictions for these compounds indicated acceptable gastrointestinal absorption and limited predicted toxicity, supporting their candidacy as orally bioavailable antidiabetic leads.

Beyond antidiabetic targets, docking of BA-linked compounds against the SARS-CoV-2 main protease (Mpro) placed Precose as the highest-scoring ligand, with a binding energy of −9.0 kcal/mol and stable interactions with catalytic residues His41, Glu166, and Asp189 confirmed by molecular dynamics simulation [Zeid, 2021]. While this finding is preliminary and isolated from the antidiabetic body of work, it demonstrates the chemical versatility of BA-associated molecules as scaffolds for computational repurposing. Across all docking studies reviewed, the convergence on carbohydrate-metabolising enzymes and metabolic signalling nodes as principal targets is consistent, and MD-validated binding stability adds a degree of credibility beyond static docking scores alone [Zeid, 2021].

Green-Synthesized Nanoparticles

Silver nanoparticles. Leaf extract-mediated green synthesis using *B. aegyptiaca* produced spherical, crystalline silver nanoparticles (AgNPs) of 10 to 20 nm diameter, with formation confirmed by UV-Vis spectroscopy, FTIR, XRD, DLS, TEM, and SEM-EDS [Dhaka et al., 2022]. These AgNPs showed antifungal activity against a phytopathogenic fungus, achieving approximately 82% radial growth inhibition and 74% spore inhibition at 150 µg/mL [Dhaka et al., 2022]. The same particles catalytically degraded methylene blue (93.47%) and Congo red (78.57%), indicating broad redox reactivity beyond biological antimicrobial applications [Dhaka et al., 2022]. In a separate study, saponin-coated AgNPs prepared from BA fruit extract produced 83 to 85% growth inhibition against HepG2 and Caco-2 cells at nontoxic doses, with stronger apoptosis-related gene modulation than crude extract under equivalent conditions. The saponin coating in the latter system served simultaneously as a stabilising agent and an active pharmacological component, a design distinction from the leaf extract-synthesised AgNPs, AgNPs where the plant material functions primarily as a reducing and capping agent [Dhaka et al., 2022].

Copper oxide nanoparticles. BA stem bark extract was used for green synthesis of copper oxide nanoparticles (CuO-NPs), with crystalline morphology confirmed by UV-Vis, FTIR, XRD, SEM, EDX, and TEM [Tekluu et al., 2023]. The CuO-NPs showed antibacterial activity against *E. coli*, *Vibrio cholerae*, *Bacillus subtilis*, and *Enterococcus faecalis*, with the largest inhibition zone of 13 mm recorded against *B. subtilis* [Tekluu et al., 2023]. The use of bark extract in this synthesis is notable given that stem bark is typically the least studied part of *B. aegyptiaca* for nanoparticle applications, and the result broadens the organ-specific utility of the plant in nanomaterial fabrication [Tekluu et al., 2023].

Polymeric Drug Delivery

Chitosan nanoparticles (CS-NPs) loaded with *B. aegyptiaca* extract represent the most pharmacologically developed delivery system studied to date. In STZ-induced diabetic rats, BA extract-loaded CS-NPs produced significantly greater reductions in fasting blood glucose and triglycerides, higher circulating insulin levels, and more substantial suppression of oxidative stress markers and pro-inflammatory cytokines than free extract administered at equivalent doses. Histological assessment showed neogenesis of pancreatic beta cells and islet regeneration in the nanoparticle-treated group. The improved outcomes are attributed to the controlled release kinetics, protection of bioactive constituents from gastrointestinal degradation, and enhanced mucosal bioavailability conferred by the chitosan matrix. This finding is particularly relevant given that the oral bioavailability of BA furostanol saponins in crude extract form remains poorly characterised, and the CS-NP data provide the first direct evidence that the formulation approach meaningfully affects in vivo antidiabetic outcomes for this plant.

Table 5. *Balanites aegyptiaca*-based nanoparticle systems: synthesis approach, particle size, characterized bioactivity, and experimental model.

Nanoparticle System	Plant Part Used	Approximate Size	Principal Bioactivity	Experimental Model
Silver nanoparticles (AgNPs)	Leaf extract	10–20 nm	Antifungal (82% radial growth inhibition at 150 µg/mL); catalytic dye degradation (methylene blue 93.47%, Congo red 78.57%)	In vitro antifungal; dye degradation assay
Saponin-coated silver nanoparticles (AgNPs)	Fruit saponin fraction	Not reported	Anticancer; 83–85% growth inhibition; enhanced apoptotic gene modulation vs crude extract	HepG2 and Caco-2 cell lines
Copper oxide nanoparticles (CuO-NPs)	Stem bark extract	Not reported	Antibacterial; largest inhibition zone 13 mm against *B. subtilis*	*E. coli*, *V. cholerae*, *B. subtilis*, *E. faecalis* in vitro
Chitosan nanoparticles (CS-NPs) loaded with BA extract	Whole plant extract	Nanoscale (not specified)	Antidiabetic; greater reduction in blood glucose, triglycerides, and oxidative stress than free extract; pancreatic β-cell neogenesis	STZ-induced diabetic rats

Saponin-coated AgNPs represent a complementary nanoplatform where the coating material is itself pharmacologically active. This system achieved selective concentration of the most antiproliferative BA saponin components at the target site and produced superior apoptotic gene modulation compared with polarity-fractionated crude extract in cancer cell models.

Future formulation strategies extrapolated from existing BA nanoparticle work include PLGA nanoparticles and phytosome-type lipid-polymer hybrids for systemic delivery of BA saponins and phenolics, though these remain untested for this plant at present.

Toxicology & Safety Profile

Acute toxicity studies across multiple preparations of B. aegyptiaca consistently indicate a wide safety margin at doses used in traditional medicine. Aqueous fruit extract produced no mortality at 5000 mg/kg oral in mice, placing its LD_{50} above this threshold [Gamde et al., 2023]. Ethanol leaf extract showed an oral LD_{50} greater than 5000 mg/kg and an intraperitoneal LD_{50} of 2154 mg/kg in rats [Sodipo et al., 2020]. A furostanol saponin-rich fraction and methanolic fruit extract were both non-lethal up to 2000 mg/kg in mice, and a phytomedicine prepared from the seed almond extract similarly had an estimated oral LD_{50} of 5000 mg/kg [Ouédraogo et al., 2025]. Seed oil and petroleum ether seed extract were non-lethal up to 5000 mg/kg, with three to four weeks of administration producing no major clinical or histopathological organ damage beyond mild kidney changes at the highest oil doses tested [Nwaogu et al., 2021].

Subacute and subchronic data present a more cautious picture at elevated doses. Aqueous fruit extract administered at 200 mg/kg for 28 days in mice caused no pathological changes, but doses of 400 to 800 mg/kg significantly elevated liver enzymes and produced hepatic and pulmonary histopathological changes. Aqueous leaf-root extract given at 250 to 1000 mg/kg for 30 days produced no clinical signs at lower doses, but at 1000 mg/kg there were measurable changes in relative heart and liver weights, mild hepatocellular degeneration, hematological shifts, and alterations in lipid profile [Ferdinand et al., 2024]. These findings collectively indicate that repeated high-dose exposure warrants caution, even when acute single-dose toxicity is low.

Figure 3: Nanoformulation Systems.

Hemolytic activity of a hydroalcoholic fruit pulp extract rich in saponins was concentration-dependent, reaching a maximum of 46% hemolysis at 12.5 mg/mL in bovine erythrocytes, interpreted by the authors as low hemolytic potential in vitro [Yapo et al., 2026]. The anti-nutritional profile of seed cake, relevant to both food and feed applications, includes saponins (1.6 to 18 mg/100 g), phytates (37 to 194 mg/100 g), tannins (0.0043 to 0.034 mg/100 g), and oxalates (15 to 350 mg/100 g), all of which can impair protein and mineral utilisation at high dietary levels [Salam et al., 2025]. B. aegyptiaca-derived selenium nanoparticles produced concentration-dependent cytogenetic changes in Vicia faba root tip cells, including altered mitotic index and chromosomal abnormalities, demonstrating genotoxic potential at the nanoparticle level that has not yet been assessed for plant extracts alone [El-Zaidy et al., 2026]. No human clinical safety trials or systematic human toxicity evaluations of B. aegyptiaca have been published. Human safety data are entirely absent from the literature, and this gap represents the most critical barrier to any clinical or regulatory progression of preparations derived from this plant.

Research Gaps, Future Directions & Conclusion

Research Gaps and Future Directions

The translational evidence base for *B. aegyptiaca* remains narrow relative to the volume of preclinical work published. A single randomised double-blind pilot trial involving 30 type 2 diabetic patients demonstrated significant improvements in glycaemic and lipid markers with a standardised pericarp extract and no reported adverse effects, but the trial authors themselves noted that controlled human studies had not been reported prior to their work [Rashad et al., 2017]. No larger or multi-centre trials have followed [Rashad et al., 2017]. This absence of robust clinical evidence is the most consequential gap in the current literature.

Extracting heterogeneity across published studies is a practical obstacle to synthesis and comparison. Aqueous, methanolic, ethanolic, and various partitioned fractions derived from different plant organs are used interchangeably across studies, with no reference to a common phytochemical standard. While one clinical formulation was standardised to stigmasterol-3-O-glucoside content [Rashad et al., 2017], no pharmacopoeial monograph or generally accepted quality specification exists for any *B. aegyptiaca* preparation, and recent reviews have explicitly identified standardisation as an unmet requirement. The human pharmacokinetics of the primary bioactive compounds, particularly the furostanol saponins and diosgenin-type aglycones, remain entirely uncharacterised. In silico ADMET predictions for balanitesin and related compounds are available, but experimental data on absorption, plasma protein binding, hepatic metabolism, and urinary or biliary excretion in any mammalian species are absent from the primary literature. Chemotypic variation within the species is documented for African material. Wood extractive profiles differ across Sahelian and Sudanian ecological zones [Dougabka et al., 2024], kernel oil fatty acid composition varies with geographic origin [Harkaoui et al., 2024], and leaf metabolomic profiles are provenance-dependent across accessions from Egypt, Sudan, Saudi Arabia, and Yemen. No comparable profiling has been conducted for Indian accessions, and direct chemotypic comparison between Rajasthan populations and African material using unified UHPLC-MS or GC-MS pipelines does not exist. Two mechanistic areas receive no attention in the available literature. Saponin biotransformation by gut microbiota and consequent effects on microbiome composition have not been examined for *B. aegyptiaca*, despite the recognised role of gut

flora in modulating saponin bioavailability and pharmacodynamics more broadly. Similarly, no study has assessed the potential for BA preparations to inhibit or induce cytochrome P450 enzymes or drug transporters, which is a relevant safety question given the plant's proposed co-administration with oral antidiabetics in traditional practice.

CONCLUSION

Balanites aegyptiaca is a chemically complex xerophytic tree whose pharmacological profile is better characterised than its clinical utility. Over 80 bioactive compounds have been identified across its organs, with furostanol saponins, phenolic acids, flavonoids, and steroidal aglycones representing the compound classes with the strongest experimental support. Antidiabetic activity is the most consistently demonstrated property, with mechanistic evidence spanning enzyme inhibition, modulation of insulin signalling pathways, and antioxidant support of pancreatic tissue across multiple independent preclinical studies. Anticancer, antimicrobial, anti-inflammatory, and hepatoprotective activities are supported by a body of in vitro and in vivo data, with balanitin-6 and balanitin-7 standing out as isolated compounds of particular potency against cancer cell lines. Computational studies have identified balanitesin as a high-affinity α-amylase inhibitor with stable binding dynamics, providing a structure-activity foundation for lead optimisation. Nanoformulation work, particularly with chitosan nanoparticle systems, demonstrates that formulation approach meaningfully improves antidiabetic outcomes in animal models beyond what crude extracts achieve at equivalent doses. Taken together, the mechanistic, in silico, and nanoformulation data position *B. aegyptiaca* as a candidate for systematic drug development. Realising that potential requires well-designed clinical trials, chemically standardised extracts, and experimental pharmacokinetic data in humans. Until those studies exist, the therapeutic promise of this plant, while scientifically credible, remains preclinical.

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