



CUSCUTA REFLEXA (AFTIMOON): A COMPREHENSIVE NARRATIVE REVIEW OF ITS ANTICANCER POTENTIAL, MOLECULAR MECHANISMS, AND THERAPEUTIC PROSPECTS

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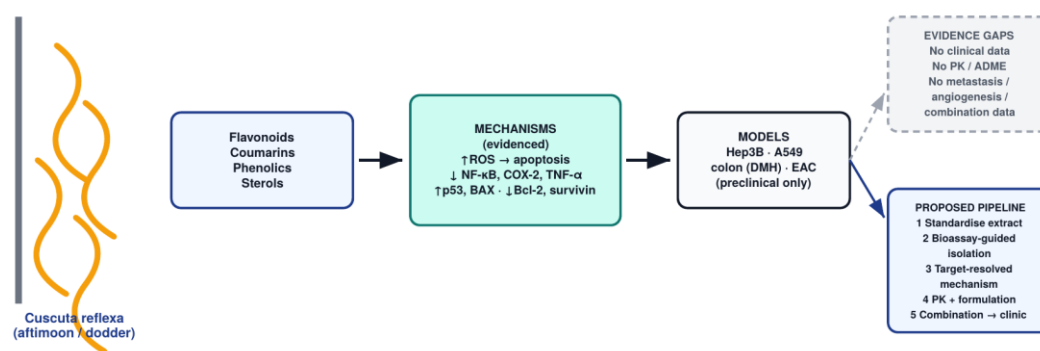
Abstract

Cuscuta reflexa (Convolvulaceae), an obligate stem holoparasite known in Unani medicine as aftimoon and vernacularly as dodder or amarbel, has a long ethnomedicinal history across South Asia for the management of tumours, jaundice, inflammation and hepatic disorders. This narrative review critically appraises the evidence for its anticancer potential and situates traditional use within contemporary pharmacology. To our knowledge, this is the first evidence-graded appraisal of the species' anticancer literature, explicitly distinguishing mechanisms that are directly demonstrated in the plant from those merely predicted or extrapolated from isolated constituents. The verifiable preclinical dataset is modest but internally coherent. An aqueous extract induced apoptosis in Hep3B hepatocellular carcinoma cells with reported up-regulation of p53 and BAX and down-regulation of Bcl-2 and survivin, alongside inhibition of nuclear factor-kappa B (NF-κB) DNA binding¹. Whole-plant chloroform and ethanol extracts prolonged survival and reduced tumour burden in Ehrlich ascites carcinoma-bearing mice². An ethanolic extract attenuated 1,2-dimethylhydrazine (DMH)-induced aberrant crypt foci in a rat colon-cancer model with a favourable hepatic safety signal³. A stem extract produced concentration-dependent, reactive oxygen species (ROS)-driven apoptosis in A549 lung adenocarcinoma cells (half-maximal inhibitory concentration, IC₅₀ ≈ 437 µg/mL),

supported by network-pharmacology predictions⁴. Activity is plausibly attributable to a flavonoid-rich matrix (kaempferol, quercetin, myricetin, luteolin, apigenin and glycosides), coumarins, phenolic acids, phytosterols and the pigment amarbelin. The recurring mechanistic themes are intrinsic (mitochondrial) apoptosis, redox modulation and suppression of NF- κ B-linked inflammatory signalling. Critically, direct species-specific evidence is absent for most pathways commonly invoked for phytochemicals (PI3K/Akt/mTOR, MAPK, STAT3, Wnt/ β -catenin, VEGF-dependent angiogenesis), and there are no data on autophagy, epigenetics, metastasis, pharmacokinetics, cancer-targeted nanoformulations, chemotherapy combinations or clinical outcomes. Methodological limitations undefined standardisation, whole-extract testing without bioassay-guided isolation, high IC₅₀ values, small cohorts and transplantable rather than orthotopic models temper current conclusions. *Cuscuta reflexa* is best described as an early-stage, mechanistically plausible but under-investigated anticancer candidate requiring standardisation, bioassay-guided fractionation, target-resolved mechanistic study, pharmacokinetic characterisation and formulation science before any translational claim.

Keywords: Cuscuta reflexa; aftimoon; dodder; phytochemistry; apoptosis; NF- κ B; reactive oxygen species; hepatocellular carcinoma; ethnopharmacology; phytopharmaceutical development.

Graphical abstract — Cuscuta reflexa anticancer potential



Mechanistically plausible, early-stage botanical oncology candidate — not a validated therapeutic.

Graphical abstract. *Cuscuta reflexa* constituents drive ROS-driven intrinsic apoptosis and NF- κ B suppression in preclinical hepatic, lung and colon models; major evidence gaps (pharmacokinetics, clinical data, metastasis, angiogenesis, combinations) and a proposed development pipeline are shown. The plant is a mechanistically plausible but early-stage candidate, not a validated therapeutic.

1. Introduction

Natural products remain central to oncology drug discovery, and a large fraction of clinically used antineoplastic agents are of botanical origin or are derived from plant metabolites.(1)Ethnomedically prioritised species offer a rational starting point, because centuries of empirical use can concentrate discovery effort onto plausibly bioactive matrices. *Cuscuta reflexa* Roxb. is one such species: a leafless, golden-yellow, obligate stem-parasitic climber of the family Convolvulaceae, distributed across the humid tropical and subtropical belts of India, Pakistan, Nepal, Bangladesh, Afghanistan, Malaysia and Thailand(2) In the Unani system it is the drug aftimoon, and communities across India, Nepal and Bangladesh have used it to treat tumours, to relieve pain and oedema, and to support hepatic function(3). The plant's inclusion in an influential early survey of Bangladeshi folk-medicine plants screened for anticancer potential⁵ provided the initial modern rationale for its study. Subsequent work

has reported anti-inflammatory, hepatoprotective, antioxidant, antidiabetic, antimicrobial and antitumour activities(3). Yet the primary experimental base specific to the species is small, and claims are often propagated across reviews without proportionate primary support. This review therefore has two aims: to synthesise and critically weigh what has actually been demonstrated, and to delineate transparently where the evidence is weak or absent, so that future work can be prioritised. We adopt a critical narrative rather than systematic approach. Studies are compared for methodological quality; conflicting or over-extrapolated findings are highlighted; and mechanistic inference from constituent phytochemicals is kept distinct from direct experimental evidence in the plant. In particular, we resist attributing to the whole plant the well-characterised anticancer pharmacology of isolated flavonoids such as quercetin and kaempferol. Those data are informative for hypothesis generation but do not constitute evidence of activity of *Cuscuta reflexa* extracts unless demonstrated as such. Although several descriptive reviews of *Cuscuta reflexa* have appeared, its anticancer literature has not previously been subjected to a structured, evidence-graded appraisal. This review is, to our knowledge, the first to explicitly separate mechanisms and signalling pathways that are directly demonstrated in the species from those that are merely predicted by network pharmacology or extrapolated from isolated constituents, presenting the distinction through evidence-coded mechanistic and signalling figures and a transparent evidence-gap matrix. In doing so it reframes the plant not as an established anticancer agent but as a mechanistically plausible, early-stage candidate, and it defines the specific, prioritised experiments required to advance it.

2. Review Methodology (Literature Search Strategy)

Although this is a narrative rather than systematic review, the search process is reported here for transparency. Literature was retrieved from PubMed, Scopus, Web of Science, ScienceDirect, SpringerLink, Wiley Online Library, MDPI, Nature, Frontiers and Google Scholar. The search combined species terms (“*Cuscuta reflexa*” OR “dodder” OR “amarbel” OR “akashbel” OR “aftimoon”) with pharmacological terms (cancer OR anticancer OR antitumour OR apoptosis OR cytotoxic OR “cell line” OR carcinoma OR phytochemistry OR flavonoid OR mechanism). Reference lists of retrieved articles and relevant reviews were hand-searched for additional primary sources.(4) The timeframe spanned database inception to 2025, prioritising studies published from 2015 onward while retaining landmark earlier reports. Only English-language publications were included, which is a recognised limitation given the plant’s use in regions where non-English literature exists. Inclusion criteria were: primary experimental studies (in vitro or in vivo) or phytochemical characterisations of *Cuscuta reflexa* with relevance to oncology. Studies on other *Cuscuta* species were retained only as congeneric context and are labelled as such throughout. Exclusion criteria were: purely agronomic or host-parasite biology reports lacking pharmacological data; secondary reviews used only for cross-referencing rather than as primary evidence; and records that could not be located in full text. Reports appearing in journals of limited editorial standing were retained but explicitly down-weighted in the appraisal. Because the review is narrative, no PRISMA flow, formal risk-of-bias scoring or quantitative meta-analysis was performed, and study selection necessarily involved author judgement. This subjectivity is itself a limitation and is acknowledged where it bears on interpretation.(5)

3. Botanical Description and Taxonomy

Cuscuta reflexa is a perennial, achlorophyllous (or minimally chlorophyllous) obligate stem holoparasite. It appears as tangled masses of smooth, wiry, yellow-to-orange twining stems bearing only vestigial scale-leaves, attaching to host stems through haustoria that penetrate host vascular tissue to withdraw water, minerals and photosynthate. Small cream-white campanulate flowers are borne in dense clusters, followed by capsular fruits and minute seeds. Vernacular names include dodder and giant dodder (English), amarbel and akashbel (Hindi) and akashavalli (Sanskrit); aftimoon denotes the Unani drug(6).

The genus *Cuscuta* comprises roughly 170–200 species(7). It was historically placed in a segregate family *Cuscutaceae*, but molecular phylogenetics supports its treatment within *Convolvulaceae*, and

modern classifications subsume *Cuscutaceae* into *Convolvulaceae*(8). This history matters for the reader, because older papers cite “*Cuscutaceae*” whereas current usage favours *Convolvulaceae*; both refer to the same taxon. A practical corollary for anticancer research is the parasitic lifestyle itself. Because the metabolite complement of a holoparasite can be influenced by the host on which it grows, host identity is a plausible and largely uncontrolled source of chemical and pharmacological variability across studies(9).

4. Ethnomedicinal Uses

Ethnobotanical records document a broad therapeutic repertoire. In Unani medicine aftimoon is used as a purgative, alterative and brain tonic, and single-drug compendia list it among agents with putative anticancer application.(10) Tribal and folk uses recorded among the Tripura community of Bangladesh and the Santar communities of Nepal include treatment of oedema and body ache, use as an aphrodisiac, maintenance of the hepatic system, alleviation of skin infections and management of jaundice. Explicit use to treat tumours in India, Nepal and Bangladesh is repeatedly cited as the traditional basis for anticancer investigation(11).

Two cautions are warranted. First, “tumour” in ethnomedical usage is semantically broad and frequently denotes swellings, goitre or inflammatory masses rather than histologically confirmed malignancy, ethnomedical endorsement therefore motivates, but cannot substantiate, an oncological indication. Second, the hepatoprotective and anticancer literatures are intertwined, with several studies reporting both. This convergence is scientifically interesting chemoprevention of hepatocellular carcinoma is a coherent hypothesis for a hepatotropic, antioxidant, anti-inflammatory botanical(12) but anti-inflammatory or hepatoprotective effects should not be uncritically relabelled as anticancer.

5. Phytochemical Composition

Preliminary screening consistently reports alkaloids, flavonoids, glycosides, phytosterols, phenolics, saponins, tannins, carbohydrates, fixed oils and proteins. Compound-level characterisation identifies a flavonoid- and coumarin-rich profile: the flavonoid aglycones kaempferol, quercetin, myricetin, luteolin and apigenin; flavonoid glycosides including astragalin (kaempferol-3-O-glucoside), hyperoside, quercetin-3-O-glucoside, kaempferol-3-O-rhamnoside, myricetin-3-O-rhamnoside and isorhamnetin-3-O-neohesperidoside; coumarins such as cuscutin, scoparone (6,7-dimethoxycoumarin) and 6-hydroxy-4-(4-hydroxyphenyl)-7-methoxycoumarin; phenolic acids (chlorogenic and caffeic acids); phytosterols (β -sitosterol, stigmasterol); the triterpene oleanolic acid, carotenoids (lycopene, lutein, violaxanthin, β -carotene, α -cryptoxanthin), the sugar alcohols dulcitol and mannitol; and the characteristic pigment amarbelin. *Cuscutalin* ($\approx 1\%$) and *cuscutin* ($\approx 0.02\%$) are frequently cited as principal stem constituents Recent phytochemical reports have reaffirmed the flavonoid-glycoside profile and quantified total flavonoid and glycoside fractions in leaf extracts(13)

Several caveats bear on interpretation. Much of the inventory derives from qualitative screening or from comparison with congeners rather than from rigorously quantified, voucher-authenticated material; absolute concentrations, batch-to-batch variation and the influence of host, season and geography are seldom reported. The name “cuscutin” is also used inconsistently (in some sources it is equated with bergenin), an ambiguity that should be resolved by explicit structural characterisation. Consequently, while the qualitative picture is robust in outline, the quantitative chemistry needed to underpin standardisation and dose–response reasoning is not yet established.(14)

Table 1. Reported phytochemical constituents of *Cuscuta reflexa* by chemical class.

Chemical class	constituents	Used part
Flavonoid aglycones	Kaempferol, quercetin, myricetin, luteolin, apigenin	Whole plant / stem

Flavonoid glycosides	Astragalin, hyperoside, quercetin-3-O-glucoside, kaempferol-3-O-rhamnoside, myricetin-3-O-rhamnoside, isorhamnetin-3-O-neohesperidoside	Whole plant
Coumarins / benzopyrones	Cuscutin, scoparone (6,7-dimethoxycoumarin), 6-hydroxy-4-(4-hydroxyphenyl)-7-methoxycoumarin	Stem
Phenolic acids	Chlorogenic acid, caffeic acid	Whole plant
Phytosterols / triterpenes	β -Sitosterol, stigmasterol, oleanolic acid, α -amyrin	Whole plant / seed
Carotenoids	Lycopene, lutein, violaxanthin, β -carotene, α -cryptoxanthin	Whole plant
Alkaloids / amides	Cuscutamine; propionamide/propenamide derivatives	Whole plant
Sugar alcohols / misc.	Dulcitol, mannitol; amarbelin (pigment); cuscutalin; fixed oils	Stem / seed

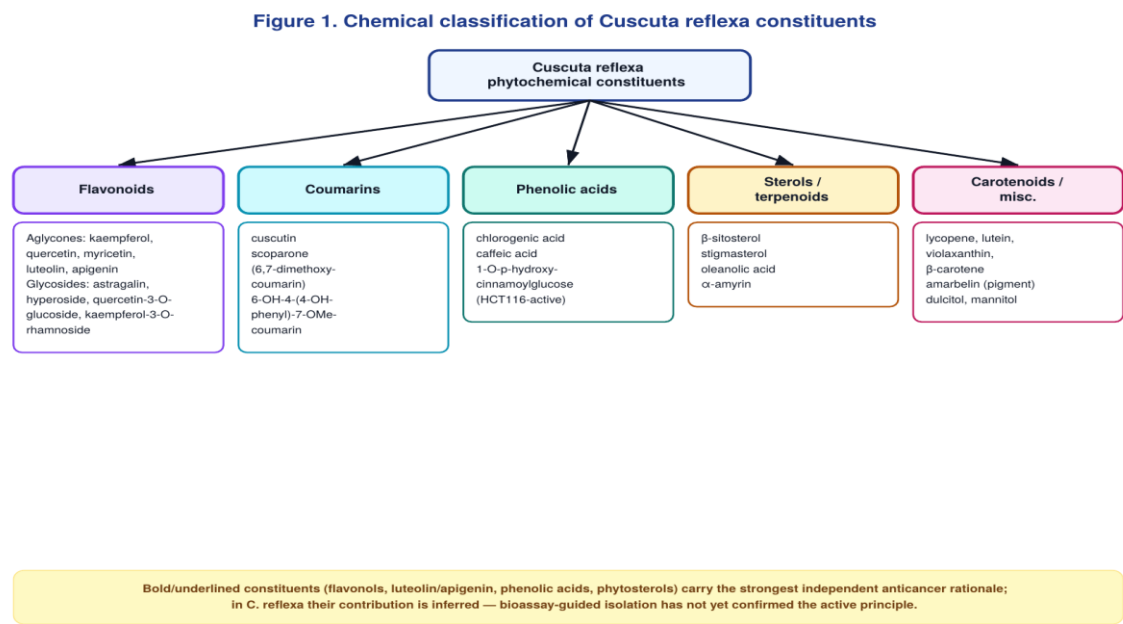


Figure 1. Chemical classification of Cuscuta reflexa constituents grouped by class. Constituents carrying the strongest independent anticancer rationale are indicated; their specific contribution to the plant’s activity remains inferential pending bioassay-guided isolation.

6. Bioactive Compounds Relevant to Cancer

The constituents most plausibly responsible for anticancer effects are the flavones luteolin and apigenin, the flavonols quercetin, kaempferol and myricetin and their glycosides, the phenolic acids chlorogenic and caffeic acid, and the phytosterols. Each has an independent anticancer literature of differing depth(15)It is this multi-constituent character that makes the matrix mechanistically credible, because parallel perturbation of several survival pathways is a recognised feature of polyphenol-rich extracts(16) A boundary must be maintained. Demonstrating that a constituent is active in isolation is not the same as demonstrating that the plant exerts that activity through that constituent. Extract

concentrations of individual flavonoids are usually low and unquantified; additive, synergistic and antagonistic interactions within the matrix are unknown; and bioassay-guided fractionation the standard method for linking a plant's activity to a molecule has scarcely been applied. One rare exception is the identification of a phenolic constituent, 1-O-p-hydroxycinnamoylglucose, with antiproliferative activity in HCT116 colorectal cells, which represents a compound-resolved anticancer observation for the plant¹². Table 2 grades constituents by the strength of their independent (compound-level) anticancer evidence and, separately, by whether that activity has been demonstrated within *Cuscuta reflexa* a distinction the review deliberately keeps visible.

Table 2. Major constituents of *Cuscuta reflexa* graded by independent anticancer evidence and by species-specific evidence.

compound	class	Independent anti cancer evidence	Evidence with cuscutta reflexa
Luteolin	Flavone	Strong	Reported constituent; not isolated as active principle
Apigenin	Flavone	Strong	Reported constituent; not isolated
Kaempferol	Flavonol	Strong	Present in extracts; activity not attributed
Quercetin	Flavonol	Strong	Present; not isolated
Myricetin	Flavonol	Moderate–strong	Reported; no plant-specific attribution
Chlorogenic acid	Phenolic acid	Moderate	Reported; plausible ROS contributor
Caffeic acid	Phenolic acid	Moderate	Reported; plausible contributor
β-Sitosterol	Phytosterol	Moderate	Constituent; no plant-specific cancer data
1-O-p-hydroxycinnamoylglucose	Phenolic	Limited (but species-specific)	Antiproliferative in HCT116 cells {{12}}
Cuscutin	Coumarin	Limited	Characteristic constituent; no cancer data
Amarbelin	Pigment	Limited	Characteristic constituent; no cancer data

7. Molecular Mechanisms of Anticancer Activity

The mechanistic base is dominated by two well-conducted studies and a few supporting reports. Each mechanism below is marked as directly evidenced, indirectly inferred, or not investigated in the species.(17)

7.1 Apoptosis

The strongest and most reproducible signal is induction of apoptosis. An aqueous extract induced apoptosis in Hep3B hepatocellular carcinoma cells shown by the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) viability assay, DAPI (4',6-diamidino-2-phenylindole) nuclear-condensation staining and annexin V labelling with transcriptional up-regulation of p53 and BAX and down-regulation of Bcl-2 and survivin. Independently, a stem extract triggered apoptosis in A549 lung adenocarcinoma cells (annexin V–propidium iodide), accompanied by increased ROS and loss of mitochondrial membrane potential . The convergence of a shifted BAX/Bcl-2 ratio, survivin suppression and mitochondrial depolarisation across two tumour types is consistent with engagement of the intrinsic (mitochondrial) apoptotic pathway.(18)

One finding warrants caution. Hep3B is widely reported as a p53-deficient (deleted) cell line(19) which makes the reported up-regulation of p53 in this model biologically difficult to interpret and in need of independent confirmation with protein-level and functional read-outs. This does not negate the apoptotic phenotype, which was demonstrated by multiple orthogonal assays, but it does illustrate why single-study transcriptional data should be treated cautiously.

7.2 Cell-cycle arrest

No study has performed cell-cycle distribution analysis (for example, propidium-iodide flow cytometry for G0/G1, S or G2/M arrest) on treated cancer cells. Arrest is plausible given the flavonoid content and reported p53 change, but this is inference, not observation, and is an easily addressable gap.(20)

7.3 Anti-proliferative activity

Concentration-dependent inhibition of viability is documented in Hep3B¹, in A549 (IC₅₀ $\approx$ 436.8 μ g/mL by sulforhodamine B), and in lower-tier reports against H-1299 and MCF-7 cells. The A549 IC₅₀ is high hundreds of μ g/mL of crude extract which is typical of unfractionated botanicals and signals limited potency of the whole extract; potency would be expected to improve with enrichment.(21)

7.4 Anti-metastatic effects

No migration, invasion, wound-healing, matrix metalloproteinase (MMP-2/9) or epithelial,mesenchymal transition (EMT) data exist for the species in cancer models. Claims of anti-metastatic potential are therefore unsupported and should not be made.(22)

7.5 Anti-angiogenesis

There are no chorioallantoic-membrane, endothelial tube-formation, HUVEC or vascular endothelial growth factor (VEGF) quantification data in an oncological context. Anti-angiogenic activity is a reasonable hypothesis for a kaempferol-containing extract but remains untested here.(23)

7.6 Oxidative-stress modulation

Extracts are consistently antioxidant in cell-free assays (DPPH, ABTS, FRAP, hydroxyl, superoxide and reactive-nitrogen scavenging), yet in A549 cells the same stem extract acted as a pro-oxidant, increasing intracellular ROS and depolarising mitochondria to drive apoptosis⁴. This apparent paradox antioxidant in chemical assays but pro-oxidant and cytotoxic in cancer cells is a recognised behaviour of polyphenol-rich matrices (24) and is one of the better-supported aspects of the plant's anticancer pharmacology.

7.7 Immune modulation and inflammation

In lipopolysaccharide-stimulated RAW264.7 macrophages, the aqueous extract down-regulated TNF- α and COX-2 and blocked NF- κ B DNA binding by electrophoretic mobility shift assay (EMSA). Given the link between chronic inflammation and carcinogenesis, this activity is relevant to chemoprevention (25)., these are macrophage data; effects on tumour immunity proper (cytotoxic T cells, natural killer cells, tumour-associated macrophage polarisation, immune-checkpoint expression) have not been studied.

7.8 Autophagy and epigenetic regulation

No autophagy markers (LC3-I/II conversion, p62/SQSTM1, Beclin-1, autophagic flux) and no epigenetic end-points (DNA methyltransferase activity, histone modification, microRNA regulation) have been examined in the species. Neither mechanism can be supported at present.(26)

Figure 2. Mechanism of anticancer action of Cuscuta reflexa — by strength of evidence

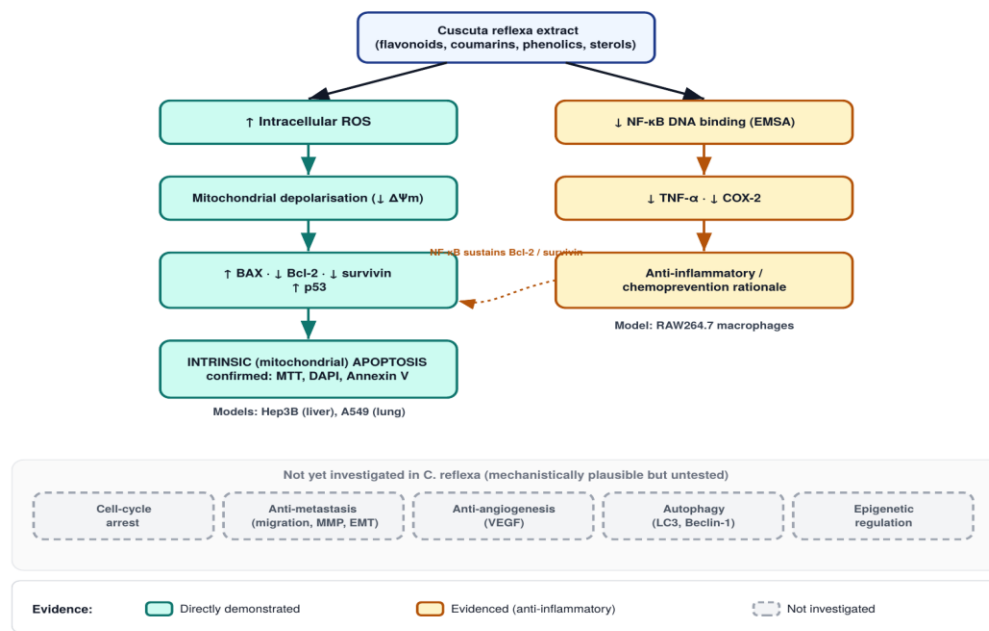


Figure 2. Mechanism of anticancer action of Cuscuta reflexa, colour-coded by strength of evidence. Solid teal denotes the directly demonstrated intrinsic-apoptosis axis ($\uparrow$ ROS $\rightarrow$ mitochondrial depolarisation $\rightarrow$ $\uparrow$ BAX/ $\downarrow$ Bcl-2, $\downarrow$ survivin, $\uparrow$ p53 $\rightarrow$ apoptosis in Hep3B and A549 cells); amber denotes the evidenced anti-inflammatory NF- κ B/TNF- α /COX-2 branch (RAW264.7 macrophages); grey dashed boxes mark mechanisms plausible but not yet investigated (cell-cycle arrest, anti-metastasis, anti-angiogenesis, autophagy, epigenetics).

8. Signaling Pathways

For integrity we separate the one pathway with direct evidence from those that are only plausible.

8.1 NF- κ B

NF- κ B is the only signalling node with direct experimental evidence in the species. The aqueous extract blocked NF- κ B binding to its DNA motifs (EMSA) and reduced downstream TNF- α and COX-2 expression in macrophages¹. Because NF- κ B also transcriptionally sustains Bcl-2 and survivin, its inhibition offers a coherent bridge to the pro-apoptotic protein changes seen in Hep3B cells(27)

8.2 p53 and the caspase/mitochondrial axis

Reported up-regulation of p53 and BAX with suppression of Bcl-2 and survivin¹, together with ROS-driven mitochondrial depolarisation, implicates the p53/BAX–mitochondrialcaspase cascade. Executioner caspase activation (caspase-3/7/9 cleavage) has not been directly measured, so caspase dependence is inferred rather than demonstrated a point compounded by the p53-status concern noted(28) in Section 7.1.

8.3 PI3K/Akt/mTOR, MAPK, STAT3, Wnt/ β -catenin, VEGF

No study has measured phosphorylation states or pathway activity for PI3K/Akt/mTOR, the MAPK cascades (ERK/JNK/p38), STAT3 or Wnt/ β -catenin, nor VEGF-dependent angiogenic signalling, in treated cancer models. Network-pharmacology analysis computationally predicts interactions between constituents and proteins implicated in lung-cancer progression, and in-silico target profiling of leaf constituents has been reported; these are hypothesis-generating predictions, not experimental pathway evidence. Statements that the plant “modulates PI3K/Akt/mTOR” or “inhibits STAT3” would currently be unsupported.(29)

Table 3. Molecular targets and signalling nodes: strength of species-specific evidence.

Target pathway	Observation in C.reflexa	Evidence status
NF-κB	Blocked DNA binding; ↓TNF-α, ↓COX-2 (macrophages)	Direct (in vitro)
p53 / BAX	Transcriptional up-regulation (Hep3B; see p53-status caveat)	Direct (mRNA-level)
Bcl-2 / survivin	Down-regulation (Hep3B)	Direct (mRNA-level)
ΔΨm / ROS	Depolarisation; ↑ROS (A549)	Direct (in vitro)
Caspase-3/7/9	Not measured	Inferred only
PI3K/Akt/mTOR; MAPK; STAT3; Wnt/β-catenin	Not measured	Not investigated / predicted
VEGF / angiogenesis	Not measured	Not investigated

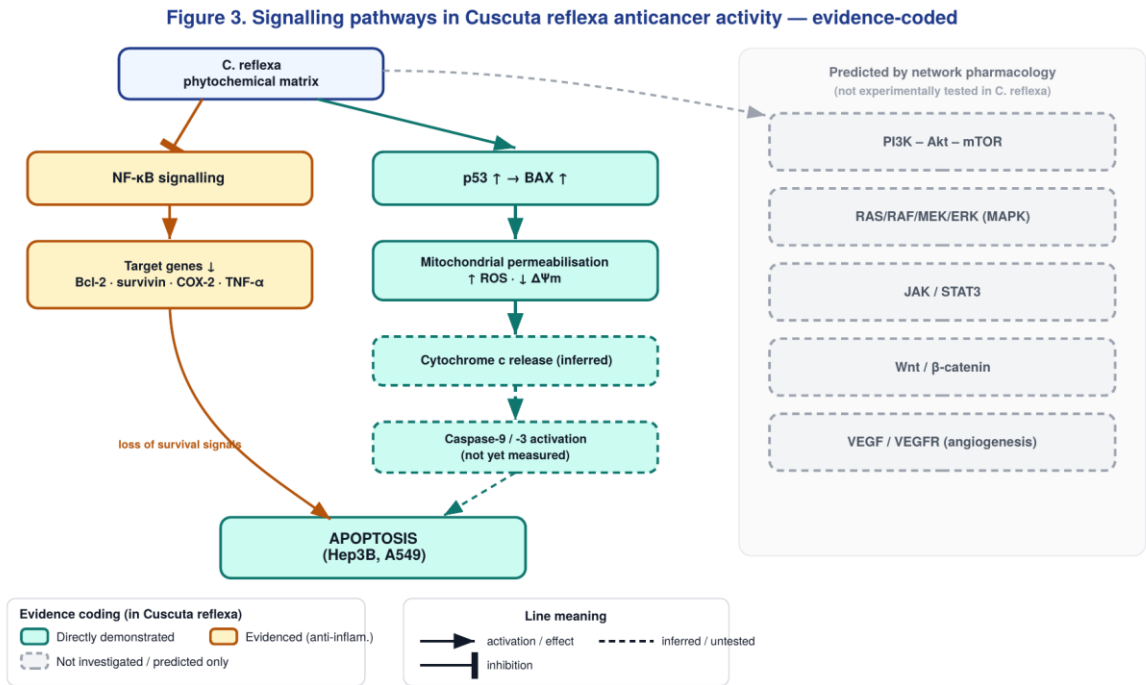


Figure 3. Signalling pathways underlying Cuscuta reflexa anticancer activity, evidence-coded. The evidenced core comprises NF-κB inhibition (amber) and the p53/BAX–mitochondrial branch (teal), with cytochrome c release and caspase-9/-3 activation shown dashed to indicate they are inferred rather than measured. PI3K/Akt/mTOR, MAPK, STAT3, Wnt/β-catenin and VEGF are grouped separately as network-pharmacology predictions. T-bar = inhibition; arrow = activation; dashed = inferred/untested.

9. In Vitro Studies

The in vitro dataset comprises a small number of studies of uneven quality. The two most rigorous the Hep3B mechanistic apoptosis and NF-κB study and the A549 ROS/mitochondrial apoptosis study, which paired sulforhodamine B and annexin V–propidium iodide assays with antioxidant testing and network pharmacology employ appropriate controls, multiple orthogonal apoptosis assays and molecular end-points. A third, lower-tier report describes cytotoxicity of extracts and flash-chromatography fractions against H-1299 (lung) and MCF-7 (breast) cells; it appears in a journal of limited editorial standing and provides weaker methodological detail, and its claim that whole extracts outperform their fractions, while plausible for a synergistic matrix, warrants caution.(30)

9.1 Comparative synthesis

Rather than reading these studies in isolation, it is more informative to ask why their read-outs diverge. Three sources of heterogeneity dominate. First, extraction solvent differs systematically: the Hep3B study used a polar aqueous extract, the lung study a stem-specific extract, and the antitumour and lower-tier studies alcohol or chloroform fractions. Because polarity governs which constituents are captured aqueous and alcoholic solvents enrich polar flavonoid glycosides and phenolic acids, whereas chloroform enriches less-polar aglycones, coumarins and sterols(31) the extracts tested are chemically non-equivalent, and apparent disagreements may reflect different molecules rather than different biology. Second, the cell lines differ in genetic background: Hep3B is p53-deficient and hepatitis-B-integrated, A549 is KRAS-mutant and p53-wild-type, and MCF-7 is hormone-receptor-positive(32) so identical extract chemistry could produce genuinely different responses, and mechanistic claims tied to p53 are model-sensitive. Third, the parasitic biology introduces uncontrolled variation in phytochemical composition with host plant, geography and season, so nominally identical preparations from different laboratories need not be comparable. Taken together, these factors mean the literature should be read as a set of concordant qualitative signals (apoptosis, ROS, NF-κB) rather than as directly comparable quantitative results; harmonised, standardised extracts tested across a common cell-line panel are needed to move beyond this.

A recurring set of limitations follows from the same causes: chemical standardisation of the tested extract is generally absent, so results are hard to reproduce or convert into dose; reported IC₅₀ values are high, indicating modest crude-extract potency; selectivity against non-malignant cells is inconsistently assessed; and bioassay-guided fractionation, which would convert these observations into defined active entities, has scarcely been undertaken.

Table 4. In vitro anticancer studies of *Cuscuta reflexa*.

Cell line(origin)	extract	Key findings	assay	refee
Hep3B (hepatocellular carcinoma; p53-deficient)	Aqueous	Apoptosis; ↑p53*, ↑BAX; ↓Bcl-2, ↓survivin	MTT, DAPI, annexin V, RT-PCR	
RAW264.7 (macrophage; inflammation model)	Aqueous	↓TNF-α, ↓COX-2; NF-κB binding blocked; no marked toxicity	RT-PCR, EMSA, viability	1
A549 (lung adenocarcinoma; KRAS-mut)	Stem	IC ₅₀ ≈436.8 μg/mL; ↑ROS; ↓ΔΨm; apoptosis	SRB, annexin V-PI, ROS, MMP	4
H-1299, MCF-7 (lung; breast)	Extracts & fractions	Cytotoxicity; extracts > fractions (claimed)	Cytotoxicity/ELISA	(lower-tier)
HCT116 (colorectal)	Phenolic constituent	Antiproliferative 1-O-p-hydroxycinnamoylglucose	Antiproliferation	12

* p53 up-regulation reported in a p53-deficient line; interpret with caution (Section 7.1).

10. In Vivo Studies

Two in vivo studies anchor the animal evidence. Chloroform and ethanol whole-plant extracts (200 and 400 mg/kg, oral) were evaluated against Ehrlich ascites carcinoma (EAC) in Swiss albino mice with 5-fluorouracil as reference; treatment reduced tumour volume and viable cell count, increased non-viable cell count and mean survival time, and restored haematological parameters toward normal, with acute oral toxicity screening indicating tolerability². More recently, an ethanolic extract was tested in a DMH-induced rat colon-cancer model, assessing aberrant crypt foci, colonoscopy and barium-enema radiography alongside histology; it attenuated tumour development and exhibited a favourable hepatic safety profile(33) (33) its survival and cell-count end-points are non-specific. The

DMH colon model is more disease-relevant and its aberrant-crypt-foci end-point is a recognised early biomarker(34) making it the more translationally informative study yet neither reports pharmacokinetics, tumour target engagement or standardised extract chemistry, so mechanistic and dosimetric interpretability is limited. No orthotopic, patient-derived-xenograft or genetically engineered mouse-model data exist.

Table 5. In vivo antitumour studies of *Cuscuta reflexa*.

Model species	Extract/part	Dose, route	Key findings
Ehrlich ascites carcinoma; Swiss albino mice	Chloroform & ethanol, whole plant	200, 400 mg/kg, oral	↓tumour volume & viable cells; ↑survival; haematology restored; tolerable in acute toxicity
DMH-induced colon cancer; Wistar rats	Ethanollic, whole plant	Oral (multi-week)	↓aberrant crypt foci; tumour attenuation; favourable hepatic safety

11. Clinical Evidence

No clinical trials of *Cuscuta reflexa* for any oncological indication were identified. There are no registered interventional studies, case series or human pharmacodynamic data for an anticancer end-point. Any statement implying clinical anticancer efficacy would be unsupported. This absence is the single most important limitation for translational framing and should be stated wherever therapeutic potential is discussed.(35)

12. Toxicity and Safety Profile

Available safety data are reassuring but preliminary. Acute oral toxicity screening in the EAC study indicated tolerability at the doses used, and the colon-cancer study reported low hepatic toxicity, consistent with the plant's documented hepatoprotective activity. Broader pharmacological studies (anti-arthritic/nephroprotective and antiemetic evaluations) have not flagged major acute toxicity.(36) However, the dossier required for a candidate anticancer phytopharmaceutical is essentially absent: there are no sub-chronic or chronic repeat-dose studies, no genotoxicity battery, no reproductive or developmental toxicology and no dose-ranged organ histopathology in an oncology context. The parasitic biology raises a specific hazard: constituents, including potentially toxic metabolites, can be acquired from the host so safety and composition may vary with host identity. Toxicological characterisation on standardised material is a prerequisite for further development.

Table 6. Toxicological observations relevant to *Cuscuta reflexa*.

Acute oral toxicity (EAC study)	Tolerated at tested doses; bracketed 200–400 mg/kg
Colon-cancer model	Low hepatic toxicity; favourable hepatic profile
Other pharmacology (anti-arthritic/nephroprotective; antiemetic)	No major acute toxicity reported
Sub-chronic/chronic, genotoxicity, reproductive tox	Not performed (gap)
Sub-chronic/chronic, genotoxicity, reproductive tox	Not performed (gap)

13. Pharmacokinetics and Bioavailability

No pharmacokinetic or bioavailability data exist for *Cuscuta reflexa* extracts or for their constituents as delivered by the plant. Absorption, distribution, metabolism, excretion and plasma exposure after oral dosing are unknown, and no experimentally validated ADMET profiling specific to an anticancer programme is available. Because several principal constituents are flavonoid glycosides with generally poor oral bioavailability and extensive first-pass and gut-microbiome metabolism(37), the

relationship between animal doses and tumour exposure is entirely uncharacterised. Without exposure data, dose response and translational claims cannot be substantiated.

14. Nanoformulations and Drug Delivery Approaches

No cancer-targeted nanoformulation studies of *Cuscuta reflexa* were found (for example, polymeric or lipid nanoparticles, nanoemulsions or phytosomes evaluated for antitumour efficacy). Nanotechnological modification of herbal products is referenced only as context in the species literature. Given the low crude-extract potency and likely poor bioavailability of the flavonoid actives, formulation science is a logical and high-value direction(38) but this section describes an opportunity, not a body of evidence.

15. Synergistic Effects with Chemotherapy

No combination or synergy studies (for example, isobolographic or combination-index analyses with cisplatin, 5-fluorouracil, doxorubicin or targeted agents) have been reported. 5-Fluorouracil served only as a comparator in the EAC study², which is not combination testing. The plant's NF-κB-inhibitory and pro-oxidant properties provide a rational hypothesis for chemo-sensitisation, because NF-κB activation is a recognised resistance mechanism(39) but this remains untested and should not be presented as an established property.

16. Multi-omics and Network Pharmacology Evidence

The principal systems-level evidence is the network-pharmacology component of the A549 study, which constructed constituent–target–pathway networks linking phytochemicals to proteins implicated in lung-cancer progression and paired these predictions with in-vitro validation. This is a strength the study did not rest on computation alone but network-pharmacology outputs are hypothesis-generating and depend heavily on the input compound list and database coverage, predicted targets are not demonstrated targets. No transcriptomic, metabolomic or single-cell datasets exist for the species in cancer, and the only proteomic anticancer work in the genus concerns the congener *Cuscuta epithymum*. Multi-omics evidence should therefore be described as nascent and predominantly in-silico.(40)

17. Molecular Docking and Computational Studies

Computational work on the species exists but is largely oriented to non-oncological pharmacology or to target prediction. In-silico profiling of identified leaf constituents has been reported alongside in-vivo pharmacology, and the network-pharmacology study incorporates target-level analysis relevant to lung cancer⁴. Docking and molecular-dynamics studies can rank candidate constituent–target pairs and guide subsequent isolation, and they are a cost-effective next step. Their known limitations scoring-function inaccuracy, static approximations and the gap between binding affinity and cellular efficacy mean docking results must be treated as prioritisation tools, not as evidence of activity.(41) No experimentally validated docking-to-bioactivity chain has yet been established for an anticancer target in the species.

18. Critical Appraisal, Challenges and Limitations

18.1 Reproducibility and standardisation

The field's central weakness is that extracts are rarely standardised. Marker-compound quantification, chemical fingerprinting (for example, HPLC or LC-MS profiles) and voucher authentication are inconsistently reported(42)so an “aqueous extract” in one study is not demonstrably the same material as in another. Without standardisation, neither positive nor negative results can be reliably reproduced, and dose cannot be defined in chemically meaningful terms.

18.2 Batch and host-dependent variability

As an obligate holoparasite, *Cuscuta reflexa* can acquire and concentrate metabolites from its host, so composition may vary with host species, geography, season and developmental stage.(43) Almost no study documents the host plant or growth conditions. This uncontrolled variability is a plausible driver of inter-study inconsistency and a specific reproducibility hazard not shared by most cultivated medicinal plants.

18.3 Extraction solvents and phytochemical selection

Because solvent polarity determines which constituents are captured, the aqueous, alcoholic and chloroform extracts tested across the literature are chemically non-equivalent (Section 9.1). Comparisons that ignore solvent are therefore comparisons of different chemical mixtures. Future work should either fix a standardised extraction protocol or, preferably, proceed to bioassay-guided fractionation so that activity is linked to defined molecules rather than to an operationally defined extract.(44)

18.4 Potency, selectivity and model validity

Reported crude-extract IC₅₀ values are high, selectivity for malignant over normal cells is under-characterised, and in vivo work relies on transplantable (EAC) or chemically induced (DMH) models rather than orthotopic or patient-derived systems. Single-study transcriptional claims exemplified by p53 up-regulation in a p53-deficient line further underline the need for orthogonal, protein-level confirmation.(45)

18.5 Translational limitations and citation amplification

There are no pharmacokinetic, formulation, combination or clinical data, so the distance from current evidence to any therapeutic claim is large. Compounding this, a meaningful fraction of the supporting literature appears in journals of limited editorial rigour, and assertions of broad “anticancer potential” are frequently repeated across reviews without proportionate primary support. Readers and reviewers should guard against this citation-amplification effect, in which the apparent weight of evidence exceeds its primary basis.

Table 7. Evidence-gap matrix for *Cuscuta reflexa* anticancer research (author synthesis).

domain	status	Priority to address
Apoptosis (intrinsic)	Directly evidenced	Confirm caspase dependence
ROS / redox modulation	Directly evidenced	Define pro- vs antioxidant switch
NF-κB / inflammation	Directly evidenced	Extend to tumour cells
Cell-cycle arrest	Not investigated	High (easy, informative)
Metastasis / angiogenesis	Not investigated	High
PI3K-Akt-mTOR/MAPK/STAT3/Wnt	Predicted only	High
Autophagy / epigenetics	Not investigated	Medium
Pharmacokinetics / ADME	Absent	Critical
Nanoformulation / delivery	Absent	High
Chemotherapy synergy	Absent	High
Clinical evidence	Absent	Prerequisite for translation

A credible development pathway should proceed as an ordered set of priorities rather than as further underpowered whole-extract screens.

Priority 1. Standardised, host-documented extracts. Establish voucher-authenticated material with recorded host, geography and season; quantify marker flavonoids and coumarins; and adopt a

reproducible extraction and chemical-fingerprinting protocol (HPLC/LC-MS). This is the foundation on which every later step depends.(46)

Priority 2 . Bioassay-guided isolation. Fractionate to resolve the active constituents the HCT116-active phenolic and the flavonoid glycosides are logical starting points converting a crude-extract literature into defined chemical entities with tractable potency and selectivity (including normal-cell comparators).(47)

Priority 3. . Pharmacokinetics and ADME. Characterise absorption, metabolism and plasma/tumour exposure of the defined actives, so that efficacious concentrations in vitro can be related to achievable exposure in vivo. Given the glycoside content, bioavailability and gut-microbiome metabolism deserve specific attention.(48)

Priority 4 . Target-resolved mechanism and rigorous in vivo models. Close the most informative mechanistic gaps first (caspase activation, cell-cycle analysis, and experimental testing not merely prediction of NF- κ B in tumour cells and of PI3K/Akt/mTOR, MAPK and STAT3), and evaluate anti-migration/invasion and angiogenesis. Confirm efficacy in orthotopic or patient-derived xenograft models with pharmacodynamic read-outs(49).

Priority 5 . Combination studies and clinical translation. Only after standardised material, defined actives, exposure data and rigorous efficacy are in hand is it responsible to pursue rational chemotherapy-combination studies (leveraging the NF- κ B/pro-oxidant rationale for chemosensitisation) and, eventually, exploratory clinical evaluation. A precision-oncology framing matching the plant's NF- κ B/redox mechanism to tumours with corresponding vulnerabilities is attractive but premature and contingent on the preceding steps.(50)

Figure suggestion (research trends): a bibliometric timeline from ~2005 (Bangladeshi folk-medicine screening) through 2011 (Hep3B and EAC studies) to 2022–2024 (colon-cancer model; network pharmacology + A549), showing the shift from ethnobotanical screening toward mechanistic and in-silico work and the persistent absence of pharmacokinetic, formulation and clinical studies.

20. Conclusion

Cuscuta reflexa (aftimoon) is a deeply embedded ethnomedicinal plant whose traditional antitumour and hepatoprotective uses have prompted a small but internally consistent body of preclinical anticancer research. The best-supported findings are the induction of intrinsic, ROS-driven apoptosis marked by a shifted BAX/Bcl-2 ratio, survivin suppression and reported p53 change in hepatocellular (Hep3B) and lung (A549) carcinoma cells, inhibition of NF- κ B-driven inflammatory signalling in macrophages, and reduction of tumour burden in Ehrlich ascites and DMH-induced colon-cancer rodent models, with an encouraging preliminary safety profile. These convergent signals across independent groups and models make the plant a mechanistically plausible anticancer candidate.(51) Equally important is what has not been shown. There is no clinical evidence, no pharmacokinetic characterisation, no formulation or combination work, and no direct experimental data on cell-cycle arrest, metastasis, angiogenesis, autophagy, epigenetics or most of the oncogenic signalling pathways routinely invoked; several such claims reflect citation amplification rather than primary demonstration, and even the available molecular data carry model-specific caveats. Realising any translational, precision-medicine or phytopharmaceutical promise will require the disciplined sequence set out above standardisation, bioassay-guided identification of actives, pharmacokinetic and target-resolved mechanistic validation, and only then combination and early-phase clinical study. Approached with this rigour and honesty about current limits, *Cuscuta reflexa* represents a worthwhile but distinctly early-stage opportunity in botanical oncology rather than a validated therapeutic.(52)

Declarations

Conflict of Interest

The authors declare that they have no conflicts of interest, financial or otherwise, in relation to this work

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Ethics Approval and Consent to Participate

Not applicable. This article is a narrative review of previously published studies and did not involve any new experiments on humans or animals performed by the authors.

Declaration of Generative Artificial Intelligence

During the preparation of this manuscript, the authors used a generative artificial-intelligence (AI) large-language-model assistant to support the literature search, to prepare an initial draft of the text, and to generate the schematic figures (Figures 1–3 and the graphical abstract, which are original vector schematics containing no copyrighted or third-party image content). No AI tool was used to generate, fabricate or alter primary experimental data, and no AI tool is listed as an author.

Data Availability

Not applicable. All data discussed in this review are available in the cited published articles.

References

1. Atanasov AG, Zotchev SB, Dirsch VM, International Natural Product Sciences Taskforce, Supuran CT. Natural products in drug discovery: advances and opportunities. *Nat Rev Drug Discov.* 2021 Mar;20(3):200–16. doi:10.1038/s41573-020-00114-z PubMed PMID: 33510482; PubMed Central PMCID: PMC7841765.
2. Chunarkar-Patil P, Kaleem M, Mishra R, Ray S, Ahmad A, Verma D, et al. Anticancer Drug Discovery Based on Natural Products: From Computational Approaches to Clinical Studies. *Biomedicines.* 2024 Jan 16;12(1):201. doi:10.3390/biomedicines12010201 PubMed PMID: 38255306; PubMed Central PMCID: PMC10813144.
3. Studies of the anticancer potential of plants used in Bangladeshi folk medicine - PubMed [Internet]. [cited 2026 Jul 13]. Available from: <https://pubmed.ncbi.nlm.nih.gov/15848015/>
4. Riaz M, Bilal A, Ali MS, Fatima I, Faisal A, Sherkheli MA, et al. Natural products from *Cuscuta reflexa* Roxb. with antiproliferation activities in HCT116 colorectal cell lines. *Nat Prod Res.* 2017 Mar;31(5):583–7. doi:10.1080/14786419.2016.1198349 PubMed PMID: 27450325.
5. KU Leuven Bibliotheken [Page] [Internet]. [cited 2026 Jul 13]. Narrative review. Available from: <https://bib.kuleuven.be/english/research/information-retrieval/review-types/narrative-review>
6. Ethanopharmacological relevance of *Cuscuta reflexa* Roxb. and its role as a hepato-protective agent: a comprehensive review | *Phytochemistry Reviews* | Springer Nature Link [Internet]. [cited 2026 Jul 13]. Available from: <https://link.springer.com/article/10.1007/s11101-025-10187-6>
7. *Cuscuta* - an overview | ScienceDirect Topics [Internet]. [cited 2026 Jul 13]. Available from: <https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/cuscuta>
8. Lin Q, Banerjee A, Stefanović S. Mitochondrial Phylogenomics of *Cuscuta* (Convolvulaceae) Reveals a Potentially Functional Horizontal Gene Transfer from the Host. *Genome Biol Evol.* 2022 Jun 14;14(6):evac091. doi:10.1093/gbe/evac091 PubMed PMID: 35700229; PubMed Central PMCID: PMC9234195.
9. Kumar K, Amir R. The Effect of a Host on the Primary Metabolic Profiling of *Cuscuta Campestris*’ Main Organs, Haustoria, Stem and Flower. *Plants.* 2021 Oct 3;10(10):2098. doi:10.3390/plants10102098 PubMed PMID: 34685907; PubMed Central PMCID: PMC8538465.

10. Khan MM, Mishra A. Unraveling the Therapeutic Potential of Miracle Plant ‘Aftimoon’ in Disease Prevention and Treatment: A Comprehensive Review. *J Drug Deliv Ther.* 2024 May 15;14(5):198–204. doi:10.22270/jddt.v14i5.6602
11. Noureen S, Noreen S, Ghumman SA, Batool F, Bukhari SNA. The genus *Cuscuta* (Convolvulaceae): An updated review on indigenous uses, phytochemistry, and pharmacology. *Iran J Basic Med Sci.* 2019 Nov;22(11):1225–52. doi:10.22038/ijbms.2019.35296.8407 PubMed PMID: 32128087; PubMed Central PMCID: PMC7038433.
12. Yeo JLS, Yong NTWM, Mahendran DCJ, Chia CLK. Approach to goitre in family medicine practice. *Singapore Med J.* 2022 Nov 18;63(10):604–14. doi:10.4103/SINGAPOREMEDJ.SMJ-2021-091 PubMed PMID: 36453431; PubMed Central PMCID: PMC9728309.
13. Aung TTT, Xia MY, Hein PP, Tang R, Zhang DD, Yang J, et al. Chemical Constituents from the Whole Plant of *Cuscuta reflexa*. *Nat Prod Bioprospecting.* 2020 Sep 21;10(5):337–44. doi:10.1007/s13659-020-00265-x PubMed PMID: 32954471; PubMed Central PMCID: PMC7520498.
14. Chakarova B, Zagorchev L, Pachedjieva K, Tosheva A, Zagorcheva T, Rusanov K, et al. Analysis of Variations in the Flavonoid Profiles of *Cuscuta campestris* and *Cuscuta epithymum* in Bulgaria as a Potential Chemotaxonomical Marker. *Plants.* 2025 Apr 16;14(8):1220. doi:10.3390/plants14081220 PubMed PMID: 40284108; PubMed Central PMCID: PMC12030255.
15. Çetinkaya M, Baran Y. Therapeutic Potential of Luteolin on Cancer. *Vaccines.* 2023 Feb 27;11(3):554. doi:10.3390/vaccines11030554 PubMed PMID: 36992138; PubMed Central PMCID: PMC10057337.
16. Chemopreventive effects of polyphenol-rich extracts against cancer invasiveness and metastasis by inhibition of type IV collagenases expression and activity - ScienceDirect [Internet]. [cited 2026 Jul 13]. Available from: <https://www.sciencedirect.com/science/article/abs/pii/S1756464618302093>
17. Papaneophytou C. Phytochemical Quorum-Sensing Inhibitors Against Bacterial Pathogens: Mechanisms of Action and Translational Challenges. *Curr Issues Mol Biol.* 2026 Feb 14;48(2):214. doi:10.3390/cimb48020214 PubMed PMID: 41751475; PubMed Central PMCID: PMC12939507.
18. Suresh V, Sruthi V, Padmaja B, Asha VV. In vitro anti-inflammatory and anti-cancer activities of *Cuscuta reflexa* Roxb. *J Ethnopharmacol.* 2011 Apr 12;134(3):872–7. doi:10.1016/j.jep.2011.01.043 PubMed PMID: 21295129.
19. Mitry RR, Sarraf CE, Wu CG, Pignatelli M, Habib NA. Wild-type p53 induces apoptosis in Hep3B through up-regulation of bax expression. *Lab Invest J Tech Methods Pathol.* 1997 Oct;77(4):369–78. PubMed PMID: 9354771.
20. Kim KH, Sederstrom JM. Assaying cell cycle status using flow cytometry. *Curr Protoc Mol Biol* Ed Frederick M Ausubel Al. 2015 Jul 1;111:28.6.1-28.6.11. doi:10.1002/0471142727.mb2806s111 PubMed PMID: 26131851; PubMed Central PMCID: PMC4516267.
21. Elsbali AM, Al-Soud WA, Mousa Elayyan AE, Alhassan HH, Danciu C, Elfaki EM, et al. Antioxidative and ROS-dependent apoptotic effects of *Cuscuta reflexa* Roxb. stem against human lung cancer: network pharmacology and in vitro experimental validation. *J Biomol Struct Dyn.* 2024;42(21):11651–76. doi:10.1080/07391102.2023.2263889 PubMed PMID: 37776015.
22. Mishra S, Alhodieb FS, Barkat MdA, Hassan MohdZ, Barkat HA, Ali R, et al. Antitumor and hepatoprotective effect of *Cuscuta reflexa* Roxb. in a murine model of colon cancer. *J Ethnopharmacol.* 2022 Jan 10;282:114597. doi:10.1016/j.jep.2021.114597
23. Parveen A, Subedi L, Kim HW, Khan Z, Zahra Z, Farooqi MQ, et al. Phytochemicals Targeting VEGF and VEGF-Related Multifactors as Anticancer Therapy. *J Clin Med.* 2019 Mar

- 12;8(3):350. doi:10.3390/jcm8030350 PubMed PMID: 30871059; PubMed Central PMCID: PMC6462934.
24. Li L, Jin P, Guan Y, Luo M, Wang Y, He B, et al. Exploiting Polyphenol-Mediated Redox Reorientation in Cancer Therapy. *Pharmaceuticals*. 2022 Dec 12;15(12):1540. doi:10.3390/ph15121540 PubMed PMID: 36558995; PubMed Central PMCID: PMC9787032.
25. Cho BO, Ryu HW, So Y, Lee CW, Jin CH, Yook HS, et al. Anti-Inflammatory Effect of Mangostenone F in Lipopolysaccharide-Stimulated RAW264.7 Macrophages by Suppressing NF- κ B and MAPK Activation. *Biomol Ther*. 2014 Jul;22(4):288–94. doi:10.4062/biomolther.2014.052 PubMed PMID: 25143806; PubMed Central PMCID: PMC4131528.
26. Mortazavi D, Sohrabi B, Mosallaei M, Nariman-Saleh-Fam Z, Bastami M, Mansoori Y, et al. Epi-miRNAs: Regulators of the Histone Modification Machinery in Human Cancer. *J Oncol*. 2022 Jan 11;2022:4889807. doi:10.1155/2022/4889807 PubMed PMID: 35087589; PubMed Central PMCID: PMC8789461.
27. Czauderna C, Castven D, Mahn FL, Marquardt JU. Context-Dependent Role of NF- κ B Signaling in Primary Liver Cancer—from Tumor Development to Therapeutic Implications. *Cancers*. 2019 Jul 25;11(8):1053. doi:10.3390/cancers11081053 PubMed PMID: 31349670; PubMed Central PMCID: PMC6721782.
28. Suresh V, Sruthi V, Padmaja B, Asha VV. In vitro anti-inflammatory and anti-cancer activities of *Cuscuta reflexa* Roxb. *J Ethnopharmacol*. 2011 Apr 12;134(3):872–7. doi:10.1016/j.jep.2011.01.043 PubMed PMID: 21295129.
29. Identification of Phytochemicals and RNA-Seq Combined in Silico Analysis of Active Compounds and Lung Cancer Related Targets of *Cuscuta chinensis* Lam - Taierpuke Maimaiti, Mourboul Ablise, Aikebaier Maimaiti, 2025 [Internet]. [cited 2026 Jul 13]. Available from: <https://journals.sagepub.com/doi/10.1177/1934578X251337225>
30. Suresh V, Sruthi V, Padmaja B, Asha VV. In vitro anti-inflammatory and anti-cancer activities of *Cuscuta reflexa* Roxb. *J Ethnopharmacol*. 2011 Apr 12;134(3):872–7. doi:10.1016/j.jep.2011.01.043 PubMed PMID: 21295129.
31. Kumar A, P N, Kumar M, Jose A, Tomer V, Oz E, et al. Major Phytochemicals: Recent Advances in Health Benefits and Extraction Method. *Molecules*. 2023 Jan 16;28(2):887. doi:10.3390/molecules28020887 PubMed PMID: 36677944; PubMed Central PMCID: PMC9862941.
32. Werner AN, Kumar AI, Charest PG. CRISPR-mediated reversion of oncogenic KRAS mutation results in increased proliferation and reveals independent roles of Ras and mTORC2 in the migration of A549 lung cancer cells. *Mol Biol Cell*. 2023 Nov 13;34(13):ar128. doi:10.1091/mbc.E23-05-0152 PubMed PMID: 37729017; PubMed Central PMCID: PMC10848948.
33. Mishra S, Alhodieb FS, Barkat MA, Hassan MZ, Barkat HA, Ali R, et al. Antitumor and hepatoprotective effect of *Cuscuta reflexa* Roxb. in a murine model of colon cancer. *J Ethnopharmacol*. 2022 Jan 10;282:114597. doi:10.1016/j.jep.2021.114597 PubMed PMID: 34492318.
34. Venkatachalam K, Vinayagam R, Arokia Vijaya Anand M, Isa NM, Ponnaiyan R. Biochemical and molecular aspects of 1,2-dimethylhydrazine (DMH)-induced colon carcinogenesis: a review. *Toxicol Res*. 2020 Mar 30;9(1):2–18. doi:10.1093/toxres/tfaa004 PubMed PMID: 32440334; PubMed Central PMCID: PMC7233314.
35. Mishra S, Alhodieb FS, Barkat MA, Hassan MZ, Barkat HA, Ali R, et al. Antitumor and hepatoprotective effect of *Cuscuta reflexa* Roxb. in a murine model of colon cancer. *J Ethnopharmacol*. 2022 Jan 10;282:114597. doi:10.1016/j.jep.2021.114597 PubMed PMID: 34492318.
36. Ali M, Khan T, Fatima K, Ali Q ul A, Ovais M, Khalil AT, et al. Selected hepatoprotective herbal medicines: Evidence from ethnomedicinal applications, animal models, and possible

- mechanism of actions. *Phytother Res.* 2018 Feb;32(2):199–215. doi:10.1002/ptr.5957 PubMed PMID: 29047177; PubMed Central PMCID: PMC7167792.
37. Batool T, Noreen S, Batool F, Shazly GA, Iqbal S, Irfan A, et al. Optimization and pharmacological evaluation of phytochemical-rich *Cuscuta reflexa* seed extract for its efficacy against chlorpyrifos-induced hepatotoxicity in murine models. *Sci Rep.* 2024 Oct 2;14:22923. doi:10.1038/s41598-024-72824-y PubMed PMID: 39358424; PubMed Central PMCID: PMC11446953.
38. Ahmad A, Tandon S, Xuan TD, Nooreen Z. A Review on Phytoconstituents and Biological activities of *Cuscuta* species. *Biomed Pharmacother.* 2017 Aug 1;92:772–95. doi:10.1016/j.biopha.2017.05.124
39. Suresh V, Sruthi V, Padmaja B, Asha VV. In vitro anti-inflammatory and anti-cancer activities of *Cuscuta reflexa* Roxb. *J Ethnopharmacol.* 2011 Apr 12;134(3):872–7. doi:10.1016/j.jep.2011.01.043 PubMed PMID: 21295129.
40. Elasbali AM, Al-Soud WA, Mousa Elayyan AE, Alhassan HH, Danciu C, Elfaki EM, et al. Antioxidative and ROS-dependent apoptotic effects of *Cuscuta reflexa* Roxb. stem against human lung cancer: network pharmacology and in vitro experimental validation. *J Biomol Struct Dyn.* 2024;42(21):11651–76. doi:10.1080/07391102.2023.2263889 PubMed PMID: 37776015.
41. Begum NF, Ramadoss R, Yadalam PK, Ramani P, Ramalingam K. Phytochemical Targeting of Nerve Growth Factor by Thymoquinone and Cuscutin: A Molecular Dynamics Simulation Study. *Cureus.* 16(7):e63727. doi:10.7759/cureus.63727 PubMed PMID: 39099944; PubMed Central PMCID: PMC11296693.
42. (PDF) Development of RAPD markers for authentication of medicinal plant *Cuscuta reflexa* [Internet]. [cited 2026 Jul 13]. Available from: https://www.academia.edu/9558511/Development_of_RAPD_markers_for_authentication_of_medicinal_plant_Cuscuta_reflexa
43. Kumar K, Amir R. The Effect of a Host on the Primary Metabolic Profiling of *Cuscuta Campestris*’ Main Organs, Haustoria, Stem and Flower. *Plants.* 2021 Oct 3;10(10):2098. doi:10.3390/plants10102098 PubMed PMID: 34685907; PubMed Central PMCID: PMC8538465.
44. Chatepa LEC, Mwamatope B, Chikowe I, Masamba KG. Effects of solvent extraction on the phytoconstituents and in vitro antioxidant activity properties of leaf extracts of the two selected medicinal plants from Malawi. *BMC Complement Med Ther.* 2024 Aug 27;24:317. doi:10.1186/s12906-024-04619-7 PubMed PMID: 39192223; PubMed Central PMCID: PMC11348721.
45. Mishra S, Alhodieb FS, Barkat MA, Hassan MZ, Barkat HA, Ali R, et al. Antitumor and hepatoprotective effect of *Cuscuta reflexa* Roxb. in a murine model of colon cancer. *J Ethnopharmacol.* 2022 Jan 10;282:114597. doi:10.1016/j.jep.2021.114597 PubMed PMID: 34492318.
46. Nortjie E, Basitere M, Moyo D, Nyamukamba P. Extraction Methods, Quantitative and Qualitative Phytochemical Screening of Medicinal Plants for Antimicrobial Textiles: A Review. *Plants.* 2022 Aug 2;11(15):2011. doi:10.3390/plants11152011 PubMed PMID: 35956489; PubMed Central PMCID: PMC9370299.
47. Gao L, Gou N, Amakye WK, Wu J, Ren J. Bioactivity guided isolation and identification of phenolic compounds from *Citrus aurantium* L. with anti-colorectal cancer cells activity by UHPLC-Q-TOF/MS. *Curr Res Food Sci.* 2022 Jan 1;5:2251–60. doi:10.1016/j.crfs.2022.11.013
48. Xiong HH, Lin SY, Chen LL, Ouyang KH, Wang WJ. The Interaction between Flavonoids and Intestinal Microbes: A Review. *Foods.* 2023 Jan 9;12(2):320. doi:10.3390/foods12020320 PubMed PMID: 36673411; PubMed Central PMCID: PMC9857828.

49. Wu X, Sun L, Xu F. NF- κ B in Cell Deaths, Therapeutic Resistance and Nanotherapy of Tumors: Recent Advances. *Pharmaceuticals*. 2023 May 24;16(6):783. doi:10.3390/ph16060783 PubMed PMID: 37375731; PubMed Central PMCID: PMC10302521.
50. Godwin P, Baird AM, Heavey S, Barr MP, O'Byrne KJ, Gately K. Targeting Nuclear Factor-Kappa B to Overcome Resistance to Chemotherapy. *Front Oncol*. 2013 May 16;3:120. doi:10.3389/fonc.2013.00120 PubMed PMID: 23720710; PubMed Central PMCID: PMC3655421.
51. Suresh V, Sruthi V, Padmaja B, Asha VV. In vitro anti-inflammatory and anti-cancer activities of *Cuscuta reflexa* Roxb. *J Ethnopharmacol*. 2011 Apr 12;134(3):872–7. doi:10.1016/j.jep.2011.01.043 PubMed PMID: 21295129.
52. Suresh V, Sruthi V, Padmaja B, Asha VV. In vitro anti-inflammatory and anti-cancer activities of *Cuscuta reflexa* Roxb. *J Ethnopharmacol*. 2011 Apr 12;134(3):872–7. doi:10.1016/j.jep.2011.01.043 PubMed PMID: 21295129.