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REVIEW ARTICLE

A Review on the Phytochemical Profile and Pharmacological Activities of the *Gossypium* Genus

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Abstract: The Gossypium genus, the source of commercial cotton, holds a significant, often-overlooked position in global ethnomedicine. While its economic value is dominated by fiber production, various parts of the cotton plant, including seeds, roots, leaves, and flowers, have a long history of use for treating a spectrum of ailments. The genus is a rich reservoir of bioactive constituents, most notably the polyphenolic sesquiterpenoid aldehyde gossypol, alongside a diverse array of flavonoids, phenolic acids, peptides, and proteins. These compounds contribute to a broad spectrum of biological activities. Scientific validation has increasingly substantiated the plant's traditional applications, revealing potent anticancer, antiprotozoal, antimicrobial, antioxidant, and anti-inflammatory properties. Gossypol, in particular, has been extensively studied as a multi-target anticancer agent. Moreover, constituents from Gossypium species and the cellulose backbone itself are being leveraged in novel material science applications, including functionalized antimicrobial textiles and advanced nanocrystal-based drug delivery systems. This review collates the ethnobotanical context, details the main phytochemical classes, organizes the current pharmacological evidence, and discusses the critical toxicological and sustainability considerations, indicating that the Gossypium genus as a valuable resource for modern therapeutic and biotechnological development.

Keywords: Gossypium; Gossypol; Phytochemistry; Pharmacological Activity; Ethnomedicine; Toxicology; Byproduct Valorization.

1. Introduction

The genus *Gossypium*, belonging to the Malvaceae family, encompasses approximately 50 species, though its global economic and cultural identity is overwhelmingly defined by the lint-producing fibers of four cultivated species: the tetraploid *Gossypium hirsutum* (Upland cotton) and *Gossypium barbadense* (Pima/Egyptian cotton), and the diploid *Gossypium arboreum* and *Gossypium herbaceum* [1]. *G. hirsutum* alone accounts for over 90% of global cotton production. While this agricultural focus on fiber is ubiquitous, it has largely overshadowed the genus's extensive history in traditional medicine systems across Asia, Africa, and the Americas [1].

Figure 1. Different species of *Gossypium*

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Historically, decoctions and extracts from cotton roots, seeds, and leaves were employed to treat conditions ranging from microbial infections and fever to inflammation and wounds [1, 2]. This ethnobotanical background has prompted modern scientific investigation, aiming to isolate the responsible bioactive compounds and validate their pharmacological effects. The primary objective has shifted from simple cataloging to mechanistic evaluation. This review consolidates the current scientific literature, moving from the core phytochemical profile of *Gossypium* species to the validated biological activities, toxicological hurdles, emerging biotechnological applications, and sustainability opportunities that stem from these natural products.

2. Phytochemical Profile of *Gossypium* Species

The biological activities of *Gossypium* extracts are a direct result of a complex mixture of secondary metabolites. These compounds vary in concentration and presence depending on the species, plant part, and environmental conditions.

2.1. Gossypol and Related Sesquiterpenoid Aldehydes

The most characteristic and extensively studied secondary metabolite in the *Gossypium* genus is gossypol, a polyphenolic, dimeric sesquiterpenoid [3]. It is primarily localized in the pigment glands of the seeds, roots, and foliage, where it functions as a phytoalexin, providing defense against pests and pathogens. Gossypol exists as two atropisomers, (+)-gossypol and (-)-gossypol, which possess different biological activities. While renowned for its toxicity and antifertility effects, which have complicated its use, gossypol and its derivatives (e.g., gossypolone, gossypin) are also the source of the plant's most potent anticancer properties [3, 4].

Table 1. Four Major Cultivated *Gossypium* Species

Species	Common Name(s)	Ploidy	Characteristics	Commercial Use
Gossypium hirsutum	Upland Cotton	Tetraploid (AADD)	Medium-staple fiber; high yield; accounts for >90% of global production.	Commercial textiles
Gossypium barbadense	Pima, Egyptian, Sea Island Cotton	Tetraploid (AADD)	Extra-long staple (ELS) fiber; high strength and fineness.	Premium textiles
Gossypium arboreum	Tree Cotton, Asiatic Cotton	Diploid (AA)	Short-staple fiber; coarse; drought and pest-resistant.	Traditional textiles, ethnobotany
Gossypium herbaceum	Levant Cotton, Syrian Cotton	Diploid (AA)	Short-staple fiber; adapted to arid climates.	Traditional textiles, ethnobotany

2.2. Flavonoids and Phenolic Compounds

Beyond gossypol, *Gossypium* species are a rich source of flavonoids and other phenolic compounds, particularly in the leaves, flowers, and bracts. These include quercetin, kaempferol, apigenin, and their various glycosides. These polyphenolics are largely responsible for the potent antioxidant and anti-inflammatory activities observed in *G. barbadense* waste extracts [4].

Table 2. Major Phytochemical Constituents of *Gossypium* Species

Phytochemicals	Examples	Plant Part(s)	Biological Activity
Sesquiterpenoid Aldehydes	Gossypol, Gossypolone, Gossypin	Seeds (glands), roots, foliage	Anticancer, Antifertility, Antimicrobial, Toxic
Flavonoids & Phenolics	Quercetin, Kaempferol, Apigenin	Leaves, flowers, bracts, hulls	Antioxidant, Anti-inflammatory, Hepatoprotective
Proteins & Peptides	Seed storage proteins, Urease, Hydrolysates	Seeds	Nutritional, Antifungal, Antioxidant
Fatty Acids (in Seed Oil)	Linoleic acid, Oleic acid, Palmitic acid	Seed kernel (oil)	Nutritional, Industrial (biofuel)

2.3. Peptides and Proteins

Cottonseed is a significant source of high-quality protein. Enzymatic hydrolysis of this protein yields bioactive peptides with considerable therapeutic potential. Specific peptide fractions from cottonseed protein hydrolysate have demonstrated high antioxidant activity [5]. Moreover, the seeds contain unique enzymes, such as urease, which possesses antifungal properties independent of its enzymatic activity, suggesting a dual defensive role [6].

2.4. Fatty Acids and Seed Oil

Cottonseed oil is one of the most significant co-products of cotton fiber production. The oil is rich in unsaturated fatty acids, primarily linoleic acid (a polyunsaturated omega-6 fatty acid) and oleic acid (a monounsaturated omega-9 fatty acid). It also contains a substantial amount of saturated fats, mainly palmitic acid and stearic acid. This fatty acid profile makes it a viable edible oil for human consumption, but only after a refining process that removes the toxic gossypol. The unrefined oil, or oil from processed seeds, also serves as a feedstock for biofuel production.

3. Pharmacological Activities and Validation

Scientific investigation has rigorously tested the traditional claims associated with *Gossypium*, leading to the validation of several main biological activities linked to its distinct phytochemistry.

3.1. Anticancer and Antitumor Properties

The anticancer potential of *Gossypium* is almost exclusively linked to gossypol. Gossypol acts as a multi-target agent, disrupting cancer cell viability through numerous mechanisms, including the induction of apoptosis and inhibition of anti-apoptotic Bcl-2 family proteins (like Bcl-2 and Mcl-1) [3]. Its ability to target multiple signaling pathways has made it a candidate for various oncologic diseases. Beyond gossypol, the plant's physical structure is also being harnessed. Cotton-derived cellulose nanocrystals (CNCs) have been functionalized with polycations to create redox-responsive platforms for the effective, targeted delivery of cancer therapeutics [7].

3.2. Antimicrobial and Antiprotozoal Activities

The traditional use of *Gossypium* species to treat infections is strongly supported by *in-vitro* data [1].

3.2.1. Antibacterial and Antifungal Activity

Extracts from various *Gossypium* species have shown efficacy against a range of human pathogens. Studies have confirmed activity against *Salmonella* species, validating their use in Cameroonian traditional medicine for typhoid fever [8]. Likewise, aqueous extracts of *G. arboreum* demonstrate inhibitory effects against bacteria such as *Staphylococcus aureus* [2]. This antibacterial action is also being exploited in material science, where cotton fabrics are functionalized with agents like frankincense oil and boric acid to impart antibacterial properties against both *E. coli* and *S. aureus* [9]. On the antifungal front, the urease enzyme isolated from *G. hirsutum* seeds has been shown to possess strong antifungal activity against plant pathogens, indicating a significant role in plant defense [6].

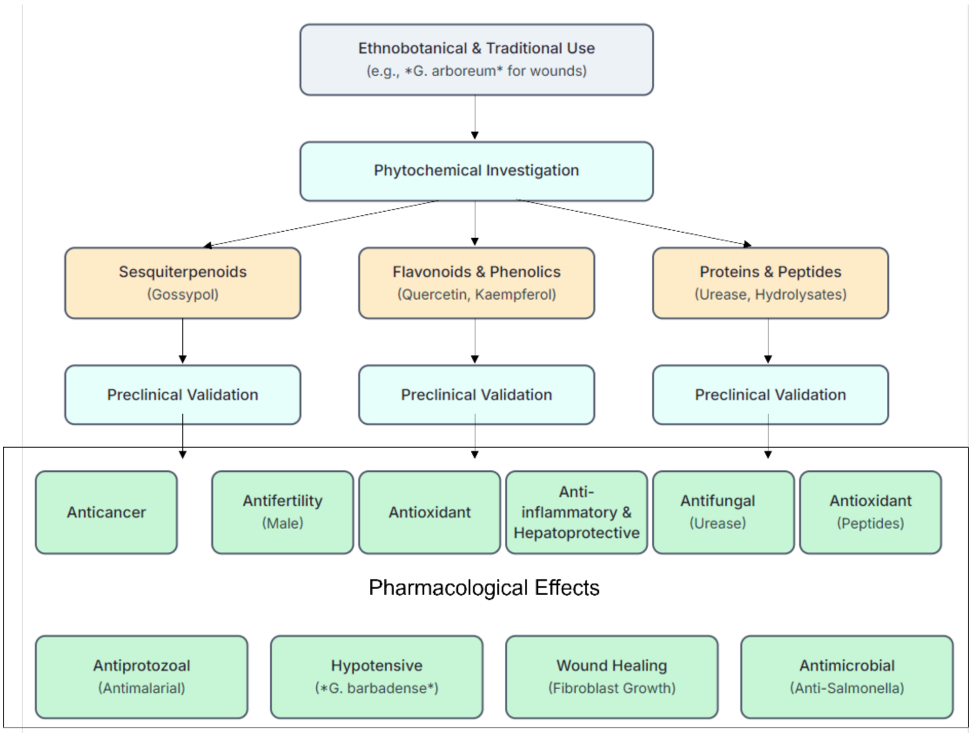

Figure 2. Pharmacological Effects of Phytoconstituents from *Gossypium* genus

3.2.2. Antiviral Activity

The inherent antiviral properties of *Gossypium* extracts are less clearly defined than their antibacterial effects. While natural products are a significant area of antiviral research [10], much of the "antiviral" activity associated with cotton involves the functionalization of the textile. For example, treating unbleached cotton nonwovens with ascorbic acid can generate antimicrobial and antiviral properties by promoting hydrogen peroxide activity, rather than through an endogenous plant compound [11].

3.2.3. Antiprotozoal Activity

One of the most promising therapeutic areas is in antiprotozoal treatment. A polyherbal remedy designated AM-1, which includes *Gossypium hirsutum*, was evaluated for malaria treatment. The remedy successfully cleared *Plasmodium falciparum* and *Plasmodium malariae* from patients' peripheral blood, with no significant adverse effects reported, suggesting a potent and well-tolerated therapeutic option [12].

3.3. Antioxidant and Anti-inflammatory Effects

Multiple studies confirm the potent antioxidant capacity of *Gossypium* extracts. Aqueous extracts of *G. arboreum* leaves protect cells from oxidative damage, a main component of wound healing [2]. This activity is attributed to the high polyphenolic content found in plant waste from *G. barbadense* [4]. These same extracts also demonstrated significant anti-inflammatory and hepatoprotective effects. The antioxidant-activity is not limited to phenolics; peptide fractions derived from cottonseed protein hydrolysate have also been identified as powerful free-radical scavengers [5].

3.4. Wound Healing Properties

The traditional use of *G. arboreum* leaves in Ghana for wound management is supported by modern pharmacological analysis. Studies show that its efficacy is likely derived from two primary mechanisms: the stimulation of fibroblast growth, which is essential for tissue repair, and a strong antioxidant effect that protects the wound bed from oxidative stress. This fibroblast-stimulating activity was found to be more significant than its direct antibacterial effect [2].

3.5. Other Systemic Effects

Beyond the major categories, *Gossypium* extracts have shown other specific systemic activities. A leaf extract of *G. barbadense*, used traditionally in Suriname for hypertension, was found to induce a dose-dependent hypotensive effect in rats. This effect appears to be mediated, at least in part, by interactions with acetylcholine receptors [13]. Additionally, extracts from *G. barbadense* agricultural waste, rich in gossypol and polyphenolics, have demonstrated significant hepatoprotective capabilities [4].

Table 3. Pharmacological Activities of *Gossypium* Constituents

Pharmacological Activity	Constituent(s)	Finding(s) & Animal Model	Reference(s)
Anticancer	Gossypol	Inhibition of anti-apoptotic Bcl-2 proteins; induction of apoptosis in various cancer cell lines.	[3, 7]
Antiprotozoal (Antimalarial)	Polyherbal extract (incl. *G. hirsutum*)	Cleared *P. falciparum* and *P. malariae* in human patients.	[12]
Antibacterial	*Gossypium* extracts; Urease	Activity against *Salmonella* sp. and *S. aureus*; antifungal properties against plant pathogens.	[1, 6, 8]
Antioxidant	Phenolics, Flavonoids, Peptide hydrolysates	Free-radical scavenging; protection of cells from oxidative damage.	[2, 4, 5]
Anti-inflammatory	Polyphenolic extracts	Demonstrated anti-inflammatory and hepatoprotective effects.	[4]
Wound Healing	*G. arboreum* aqueous extracts	Stimulation of fibroblast growth and antioxidant protection in wound models.	[2]
Hypotensive	*G. barbadense* leaf extract	Dose-dependent reduction in blood pressure in rats; likely via cholinergic receptors.	[13]

4. Current Applications in Material Science

The utility of *Gossypium* is no longer limited to pharmacology or simple textiles. Modern material science is exploiting both the chemical and physical properties of cotton.

4.1. Functionalized Multifunctional Textiles

Cotton fabric serves as an ideal, renewable substrate for functionalization. Researchers have successfully applied microcapsules containing boric acid, chitosan, and frankincense oil to cotton fabric. The resulting textile gained multiple properties simultaneously: 100% mosquito repellency, significant antioxidant activity, antibacterial efficacy, and flame retardancy [9]. Other processes, such as treatment with ascorbic acid, can impart antimicrobial and antiviral properties to spunlace nonwovens, making them suitable for medical applications like wound dressings and barrier fabrics [11].

4.2. Nanotechnology and Drug Delivery

At the nanoscale, cotton-derived cellulose nanocrystals (CNCs) offer a biocompatible and tailorable platform for advanced therapeutics. By functionalizing these CNCs, scientists have developed sophisticated drug delivery systems. One such system, based on redox-responsive polycation-functionalized CNCs, is designed specifically for targeted cancer treatment, enhancing the efficacy and precision of the therapeutic payload [7].

5. Toxicology and Safety

A detailed assessment of *Gossypium* must include its significant toxicological challenges, which primarily stem from gossypol and common fungal contaminants.

5.1. Gossypol-Induced Toxicity and Antifertility

Gossypol is the plant's primary chemical defense, and it is inherently toxic to most non-ruminant animals and humans. At high doses, it is cardiotoxic and hepatotoxic. Its most widely documented effect, however, is as a male antifertility agent. This property was discovered in China in the 1970s, where crude cottonseed oil in the diet was linked to widespread male infertility. Mechanistic studies revealed that gossypol inhibits sperm-specific enzymes (like lactate dehydrogenase-X) and disrupts spermatogenesis, leading to immotile sperm or azoospermia [14]. While this spurred research into gossypol as a potential male contraceptive, clinical trials were largely halted due to issues with irreversible infertility in some subjects and systemic toxicity, particularly hypokalemia. This toxic profile is the single greatest barrier to the widespread use of cottonseed as a direct food source [15].

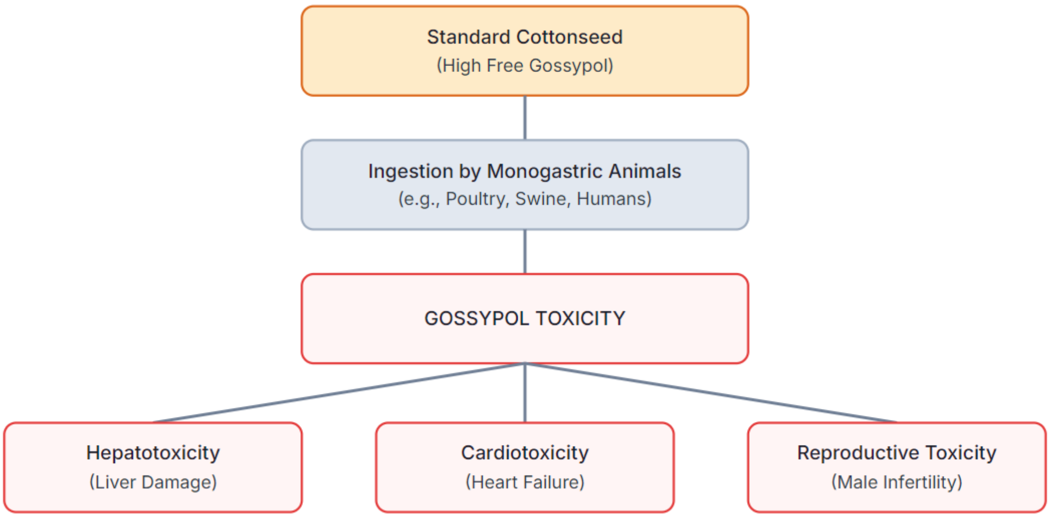

Figure 3. Toxicity of Gossypol

5.2. Aflatoxin Contamination in Byproducts

A separate but equally severe safety concern is the contamination of cottonseed products, particularly cottonseed meal, with aflatoxins. *Aspergillus flavus* and *Aspergillus parasiticus* are fungi that can colonize cotton bolls in the field, especially under warm, humid conditions. These fungi produce aflatoxins, which are among the most potent naturally occurring carcinogens and hepatotoxins known. When contaminated cottonseed cake is fed to livestock, it can cause severe illness and reduced productivity. Moreover, aflatoxin metabolites can pass into the milk of dairy cattle (as aflatoxin M1), posing a direct threat to human health [16].

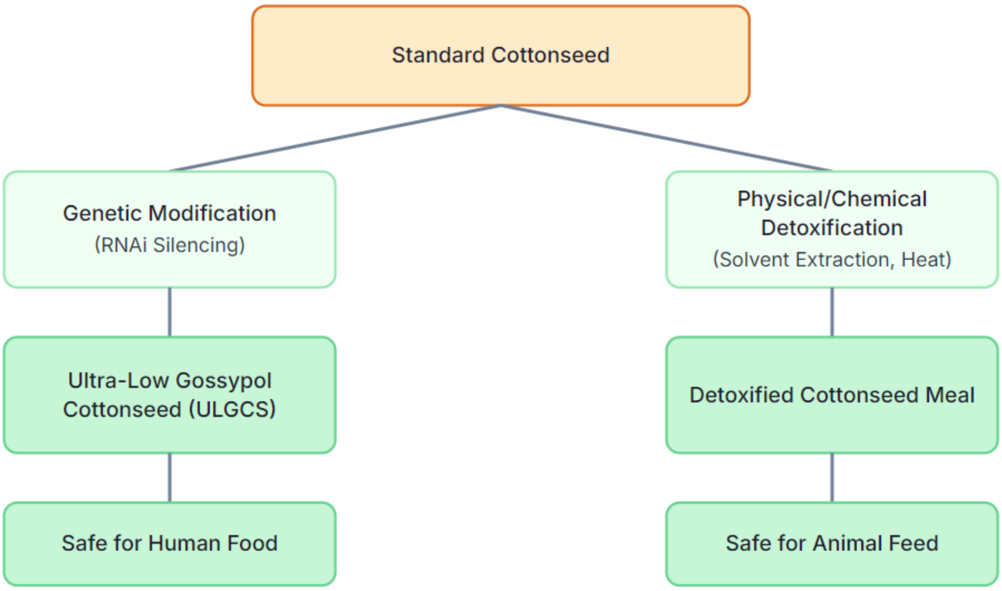

Figure 4. Mitigation Techniques for Reducing Toxicity of Gossypol

6. Sustainability and Byproduct Valorization

The cotton industry generates massive quantities of non-fiber biomass. The effective use of this "waste" stream, often referred to as valorization, is a critical component of a sustainable and economically viable cotton industry.

6.1. Cottonseed as a Protein and Oil Resource

For every kilogram of fiber, the cotton plant produces approximately 1.6 kilograms of seed. This seed is a rich resource, containing high-quality protein (20-25%) and oil (20-22%). As discussed, the oil is a major commercial product. The remaining cottonseed meal, or cake, is a primary component of animal feed, especially for ruminant animals (like cattle) which can detoxify the gossypol in their rumen. The toxicity issues (gossypol and aflatoxin) are the main limitations on its broader use [17].

Table 4. Major Byproducts of Cotton Processing and Their Valorization

Byproduct	Primary Components	Traditional Use / Low-Value Application	High-Value Valorization / Potential
Cottonseed	Oil (~20%), Protein (~22%), Gossypol	Crushing for unrefined oil; feed for ruminants.	Food-grade edible oil (refined); high-protein meal (for ULGCS) for human/monogastric nutrition.
Cottonseed Meal / Cake	Protein (~40-50%), Fiber, Residual Gossypol	Animal feed (primarily ruminants).	Source of bioactive peptides; aquaculture feed; high-protein food additives (from ULGCS).
Cotton Linters	High-purity Cellulose (>98%)	Low-grade padding, paper.	Production of rayon, carboxymethyl cellulose (CMC), nanocellulose, bioplastics, drug delivery systems.
Hulls	Lignocellulose, Fiber	Roughage in animal feed; boiler fuel.	Substrate for industrial fermentation; mushroom cultivation; source of phenolic compounds.
Stems, Leaves & Gin Trash	Lignocellulose	Burned for energy; left in field.	Biofuel (ethanol) production; composite board manufacturing; source of bioactive extracts.

6.2. Valorization of Lignocellulosic Residues (Hulls and Stems)

The lignocellulosic byproducts of cotton processing are also significant. Cottonseed hulls (the outer covering of the seed) are separated during oil extraction and are often used as a source of roughage in animal feed or as a substrate for industrial fermentation. The short fibers remaining on the seed after ginning, known as linters, are a high-purity source of cellulose, which is a valuable precursor for producing chemicals like carboxymethyl cellulose (CMC), rayon, and other polymers. The stems, leaves, and bracts (gin trash) are typically left in the field or used as low-grade biomass for energy production (combustion) or composting.

6.3. Genetic Engineering for Low-Gossypol Seed

The primary obstacle to unlocking the full nutritional value of cottonseed is gossypol. This has driven significant research in genetic engineering. By using RNA interference (RNAi) technology, scientists have successfully "silenced" the genes responsible for gossypol production specifically in the seed, while maintaining normal gossypol levels in the rest of the plant (leaves, stem, roots) to preserve its natural pest resistance. This "Ultra-Low Gossypol Cottonseed" (ULGCS) has been approved for human consumption and animal feed in several countries. This development has the potential to transform cottonseed from a toxic byproduct into a high-protein, globally significant food and feed source, addressing nutritional security and dramatically increasing the crop's value[18].

7. Conclusion

The *Gossypium* genus represents a striking example of a plant with a dual identity. While it underpins the global textile industry, it is also a profound reservoir of bioactive compounds with a rich ethnobotanical history. The scientific evidence strongly supports its traditional uses, showing potent anticancer, antiprotozoal, antibacterial, antioxidant, and anti-inflammatory activities. The toxicity of its hallmark compound, gossypol, remains a significant hurdle—both for its clinical application and for the use of cottonseed—but it is also the source of its most powerful anticancer effects. Research into derivatives and targeted delivery systems continues to mitigate these toxicological concerns. Moreover, the sustainable valorization of *Gossypium* byproducts is at a turning point. Genetic advances that remove toxins from the seed without compromising the plant's natural defenses may unlock a new, massive source of protein for global food security. The combination of cotton-derived materials into advanced applications, from functional fabrics to nanomedicine, signals a new era for this ancient and versatile plant.

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