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Unlocking the Nutraceutical Potential of Adlay (*Coix lacryma-jobi L.*): Prospects and Applications

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ABSTRACT

Adlay (*Coix lacryma-jobi* L.) is a cereal containing nutrients and bioactive compounds that provide various health benefits. However, exploration of adlay's potential as a nutraceutical and wider applications has not been widely discussed. Therefore, this review aimed to comprehensively explore the nutraceutical potential, applications, and future prospects of adlay based on literature published in the past five years. Literature searches were conducted online using databases such as Scopus, Google Scholar, and Lens with keywords such as "nutraceutical AND adlay," "adlay OR coix phytochemical," "adlay OR coix functional foods," "adlay OR coix pharmacological activities," "adlay OR coix traditional use," "adlay OR coix formulation," and other relevant keywords. The results showed that adlay contained various components capable of being further developed for nutraceutical products, such as starch, fiber, coixan, arabinoxylan, and various bioactive compounds. Adlay was also reported to be developed as a nutraceutical to improve the nutritional content of products. Various applications that had been explored in pharmaceutical preparations included microemulsions, liposomes, and nanostructured-lipid carriers, with synergistic results for cancer treatment. This suggested that adlay could serve as a nutraceutical product, functioning as a nutritional enhancer, an oil that synergizes with anticancer drugs, and an extract with antidiabetic effects, among others. Consequently, adlay was identified as a plant with substantial potential for further development in nutraceutical products and pharmaceutical formulations.

Keywords: adlay, *coix lacryma-jobi*, nutraceutical, applications, food, pharmaceutical

INTRODUCTION

Nutraceutical products are experiencing significant growth in the global market, with sales reaching USD 383.69 billion in 2022 and projected to expand at an annual growth rate of 9.5% from 2024 to 2031 (Bose & Sharma, 2025). This rising popularity is largely driven by increasing public awareness of health maintenance, particularly in the post-pandemic era. Moreover, the nutraceutical concept that uses safe bioactive food components with pharmacological activity has attracted considerable interest. The growing consumer preference for natural products, influenced by the "back to nature" movement, has further stimulated demand for naturally derived nutraceuticals, showing their vast potential and promising future prospects (Azzahra, Astuti, et al., 2024; Setiawan et al., 2024). The high demand poses a challenge to the continuous exploration of new potential nutraceuticals. Furthermore, global warming is a concern that requires consistent diversification of nutraceutical sources. Naturally derived nutraceutical products have been extensively developed, ranging from crude extracts to isolated bioactive compounds obtained from various food groups such as grains, fruits, vegetables, and other

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plant-based materials (Azzahra, et al., 2024; Rawat et al., 2023). Examples of natural extracts used in nutraceutical formulations include garlic, carrots, and red yeast rice (Drugs.com, 2025; Multum, 2023). Additionally, several bioactive compounds have been isolated from food sources for nutraceutical applications, including lycopene, anthocyanins, astaxanthin, omega-3 fatty acids, and others (Azzahra, et al., 2024). Among the diverse natural sources investigated, cereals such as wheat, corn, sorghum, millet, barley, adlay, and oats, as well as pseudo-cereals, have shown significant potential for nutraceutical development (Chaturvedi et al., 2011; Rawat et al., 2023).

Adlay, known as adlay millet, hanjeli, jali, or coix (*Coix lacryma-jobi* L.), is a cereal native to Southeast Asia, including Indonesia. Historically, it has been consumed as food (Andriana et al., 2023; Budiman & Wardani, 2021; Zhu, 2017) and used in traditional medicine (Chen et al., 2022). Despite the rich nutritional profile, adlay remains an underutilized cereal, which has received less attention compared to other staple grains such as maize, wheat, and sorghum. Previous studies have shown the nutritional content of adlay, such as high protein, low-calorie carbohydrates, and unsaturated fatty acids, with potential as nutraceuticals (Igbokwe et al., 2021; Li et al., 2024; Zhu, 2017). This cereal has also been reported to contain various bioactive compounds beneficial to health. However, there is limited information on the potential and applications of adlay, particularly in supporting the role as a nutraceutical. This includes the use as oil, extract, or broader potential applications, despite the significant global demand for raw materials. In cultivation, adlay is more tolerant of harsh conditions, such as laterite soil and low pH, compared to corn, with high resistance to virus attacks (Zhu, 2017). It also produces 2-4 tons per hectare, with a milling percentage (several seeds that have been peeled), and clean grains generate 30-50% (Aqil et al., 2023). Another advantage is that, along with increasing studies, reports on better productivity are continuously being carried out, making adlay a potential in terms of sustainability.

Previous studies exploring nutraceutical potential of adlay have primarily focused on genetic resources and bioengineering. For example, Huda et al. (2023) reviewed germplasm and genetic engineering methods, such as genome sequencing, to develop nutrient-rich, superior adlay seeds. Qosim et al. (2023) examined seed productivity, emphasizing the sustainability and potential for long-term product development. Weng et al. (2022) conducted a review on adlay as a nutraceutical by focusing on genome sequencing and some nutritional properties. However, studies regarding the nutraceutical potential, including its applications, remain limited. Based on the knowledge gap, this review aims to explore the nutraceutical potential of adlay, including the comprehensive nutraceutical properties, applications, and future prospects for development as a nutraceutical product. This review is based on relevant literature, focusing on studies related to the use of adlay in both food and pharmaceutical products over the past five years. The literature search is conducted online using databases such as Scopus, Google Scholar, and Lens, with keywords such as “nutraceutical AND adlay OR coix,” “adlay OR coix phytochemical,” “adlay OR coix functional food,” “adlay OR coix pharmacological activities,” “adlay OR coix traditional use,” “adlay OR coix formulation,” and other relevant terms.

INSIGHTS FROM PREVIOUS STUDIES OF ADLAY

Based on data from Lens.org, scientific studies related to coix or adlay comprised 3,127 datasets and 19,591 patents. The highest number of publications was recorded in 2023, with 141 studies and 82 datasets, while patent filings containing the keyword Coix peaked in 2016, reaching 2,071 patents (Lens, 2025; Scopus, 2024).

Compared to the broader search results from Lens.org, a more specific query using the keyword "Coix" (the commonly used Latin term for adlay) in the Scopus database showed a steady increase in studies on adlay since 2018, with 42 publications. This trend culminated in 2024, with a peak of 122 publications. The results showed a growing interest in exploring the potential applications of adlay, particularly in the fields of medicine and pharmaceuticals (Figure 1) (Supplement 1).

This review primarily draws on recent literature on the use of adlay, both in the authors' home country, Indonesia, and internationally, showing a significant increase in studies in recent years. The trend suggests that in the coming years, broader studies on adlay will further expand the knowledge base beyond this review, potentially leading to wider applications in the health sector.

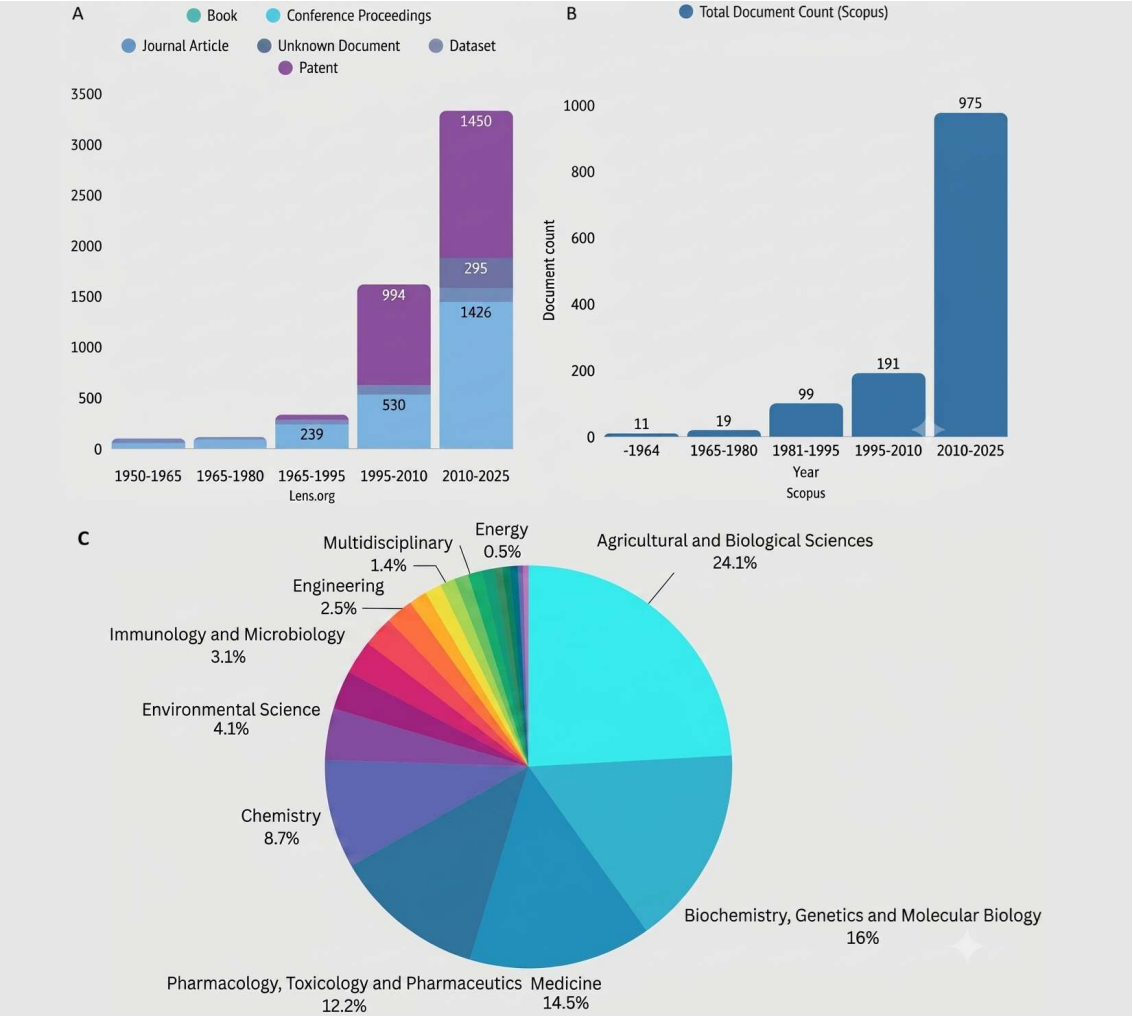


Figure 1. Analytical results from various data sources, including (a) Lens.org and (b) Scopus search, show an increasing trend in the publication of scientific articles related to adlay. In addition, (c) data from Scopus regarding documents by subjects shows that coix is underdeveloped in the pharmaceutical area.

Nutraceutical is at the intersection between food (nutrition-related aspects) and pharmaceuticals (therapeutic/pharmacological effects). However, existing studies on adlay are predominantly categorized under food science and pharmaceuticals, with limited exploration of the nutraceutical potential.

DRAW THE LINE: ADLAY AS NUTRACEUTICAL

The term "nutraceutical" was first introduced in 1989 by Stephen De Felice to describe foods or food-derived components with pharmacological effects (Aronson, 2017). Closely related to nutraceutical, the terms "functional foods" and "dietary supplements" were also used to denote food-based substances intended to enhance health.

The concept of functional foods became prominent in the 1980s and was formally defined in 1991, while dietary supplements were officially classified in 1994. Over time, the definition of functional foods has gained significant attention, consistently referring to foods specifically formulated to confer additional nutritional or health benefits through ingredient enrichment or fortification (Egbuna & Dable-Tupas, 2020).

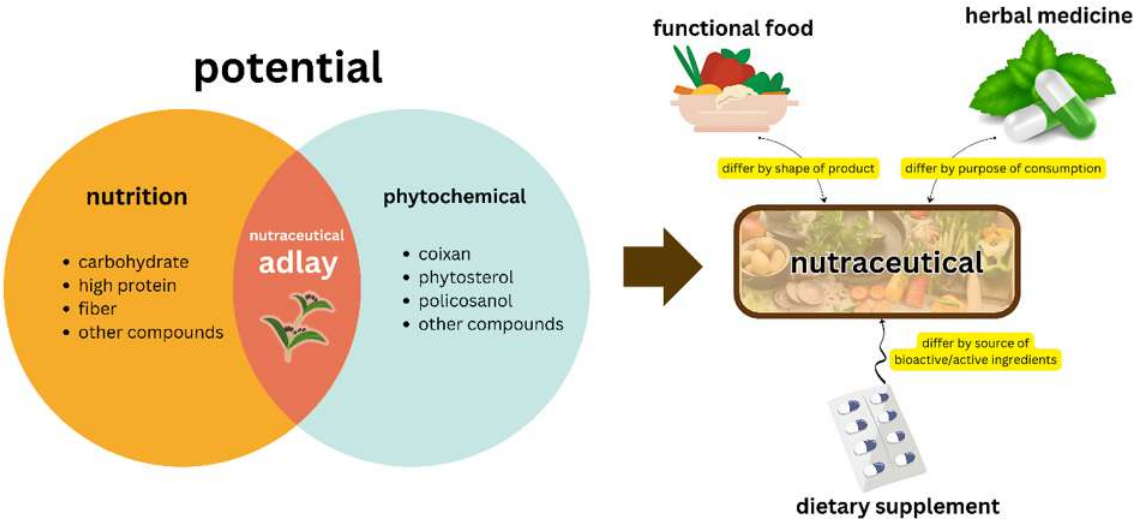


Figure 2. Adlay shows both potential to be developed as nutraceuticals, which combine food and medicine properties.

In comparison, dietary supplements have long been recognized as consumable products containing "dietary compounds" designed to complement the diet. The regulatory classification of supplements has progressively expanded to accommodate "new dietary compounds" that meet established safety and efficacy standards (Aluko, 2012, pp. vii-viii; Food and Drug Administration, 2024; Gupta, 2016).

The overlapping purposes of nutraceutical, functional foods, and dietary supplements in promoting health and preventing disease have led to ambiguity, causing debate and differing opinions. Some of the key controversies include questions such as, *"If all three serve the same purpose, why use different terms?"* or *"Should they be categorized the same despite their differences?"* While these terms share similarities, they also have distinct characteristics, though some sources fail to provide clear boundaries.

To clarify these distinctions, this review summarizes and proposes explicit definitions, particularly for closely related terms (Figure 2). The illustrations show the similarities and differences between nutraceutical, functional foods, dietary supplements, and herbal medicines, focusing on delineating dietary supplements and nutraceuticals. As the diversity of products and studies in this field continues to grow, establishing precise categorical definitions will be essential in guiding product development and ensuring clarity in scientific discourse. The Indonesian Functional Food and Nutraceutical Activists Association (*Perhimpunan Penggiat Pangan Fungsional dan Nutrasetikal Indonesia*, P3FNI) defined nutraceutical as "Food components that are safe for consumption and provide health benefits beyond the essential functions of regular nutrients, as supported by scientific evidence. These components are present in amounts exceeding natural occurrence in food to exert their benefits and are shown in a non-food matrix" (P3FNI, 2023).

As the root of the word nutraceutical is nutrition and pharmaceutical or phytochemical, adlay includes two categories of applications that can be optimized in its role as a nutraceutical (Figure 2). For nutrition, adlay contains 65% carbohydrates, 14% protein, 3% crude fiber, 5% fat, 0.242% phosphorus, 0.07% calcium, and 0.001% iron (Igbokwe et al., 2021). The carbohydrate content consists of starch approximately 60-70% (Zhu, 2017), non-starch polysaccharides of 4-8% (Hu et al., 2022), oligosaccharides 25% (Manosroi et al., 2014), and dietary fiber of 1.3-3% (Liu et al., 2015).

The nutrient composition of adlay has been compared with other grains, such as maize, millet, rice, and sorghum. The result shows that adlay has highest protein (14.1%) and lipid (7.9%) content compared to other grains. Additionally, various parts have been explored for their macro- and micronutrient content, as well as bioactive compounds. A comparative analysis of the nutrient composition across different parts of adlay plant reported that starch content was highest in the

seeds (48.58%), followed by the seed testa (3.5%), seed shell (4.56%), roots (6.78%), stems (8.89%), and leaves (3.21%). Similarly, protein content was found to be highest in the seeds (19.33%), followed by the roots (19.06%), leaves (18.29%), and stems (12.07%). In comparison, fat content was highest in the roots (7.15%), followed by the seed testa (5.31%) and seeds (4.7%) (Zeng et al., 2022).

Regarding the phytochemical potential which can be used as medicine, adlay contains bioactives in the form of policosanols (docosanol, tetracosanol, hexacosanol, and octacosanol), phytosterols (squalene, campesterol, tocophenol, ergostanol, and β-sitosterol), polyphenols (coniferyl alcohol, syricic acid, ferulic acid, syringaresinol, 4-ketopinoresinol, p-hydroxy benzaldehyde), flavonoids (apigenin, luteolin, quercetin, kaempferol, naringenin, nobiletin, tangeretin, isoliquiritigenin, eriodictyol, formononetin and rutin), lignans, neolignans, spiroenone, lactams, and spirolactam (Devaraj et al., 2020).

UNLOCKING NUTRACEUTICAL PROPERTIES OF ADLAY

Adlay, also known as hanjeli (*Coix lacryma-jobi L.*), is a cereal crop native to Southeast Asia, including Indonesia, and has long been consumed as a food source (Andriana et al., 2023; Budiman & Wardani, 2021; Zhu, 2017). The most extensively studied part is the seeds, which are rich in both macronutrients and micronutrients. However, further investigation showed that adlay potential was not only in the seeds but in other parts.

Starch

Starch is a biopolymer commonly found in many plants, primarily composed of amylose and amylopectin. Amylose is a linear polymer with minor branching, consisting of glucan chains linked by α-(1→4) bonds, with a molecular weight typically ranging from 10^5 to 10^6 Da. In comparison, amylopectin is a highly branched polymer, containing short glucan chains linked by α-(1→4) bonds and α-(1→6) bonds at branching points, with an average molecular weight between 10^7 and 10^9 Da (Sui & Kong, 2018).

The amylose content in common adlay ranges from 15.9% to 25.8%, while glutinous has a lower value of approximately 0.7–1.1%. Generally, the swelling power of glutinous adlay starch is higher (28.6–41.0 g/g) compared to glutinous maize starch. Regarding gelatinization temperature, normal adlay starch shows a higher peak temperature (71.1°–71.4°C) compared to normal maize starch (71.9°–75.5°C), resembling that of glutinous maize. The Rapid Visco Analyzer (RVA) profile of normal adlay starch shows similarities to normal maize starch. Meanwhile, the RVA profile of glutinous adlay starch shows greater variability and a lower peak viscosity compared to glutinous maize starch (Wrigley et al., 2016).

Glutinous adlay starch forms a relatively soft gel, while the hardness of normal adlay starch ranges from 11.4 to 31.1 g. The gelatinization temperature of glutinous adlay starch varies between 63.4°C and 76.4°C, with a water-binding capacity of 103–108%. The starch content in the grains averages 45%, with birefringence loss in starch granules occurring between 65°C and 75°C. Moreover, significant degradation is observed during pasting using a Brabender Visco-Amylo-Graph, showing high thermal sensitivity. The physicochemical properties of glutinous adlay starch closely resemble those of glutinous maize starch, with amylose content being the primary determinant of functional differences (Wrigley et al., 2016).

With a high starch content (60–70%), adlay seeds can serve as fillers, binders, or disintegrants in tablet and capsule formulations. This application is in line with the general use of starch in pharmaceutical. However, further processing or modification of adlay starch, including physical, chemical, or enzymatic modification, can alter the functional properties to meet specific formulation requirements.

Pregelatinization is a widely recognized physical modification method that enhances water absorption and viscosity, particularly at room temperature. This makes pregelatinized starch an effective binder, capable of forming a uniform matrix upon hydration (Sui & Kong, 2018). Additionally, heat-moisture treatment (HMT), including annealing or alternative methods, reduces swelling capacity and water absorption (Gebremedhin & Admassu, 2022; Sui & Kong, 2018), serving as a promising method for controlled-release formulations depending on the desired functional properties. In comparison, freeze-moisture treatment (FMT) combined with ozonation, as reported by Subroto et al. (2022), led to high water absorption, volume expansion, solubility, increased porosity, and amorphous structure formation. These observed effects are similar to pregelatinization, without introducing new functional groups.

The amylose-to-amylopectin ratio and unique physicochemical properties of adlay starch hold promising potential for nutraceutical product development. However, studies on adlay starch applications in pharmaceutical formulations remain limited. Igbokwe et al. (2021) emphasized that the functional benefits of adlay largely occurred from the starch content, suggesting the potential as an excipient in nutraceutical formulations. Further pharmaceutical studies and development are required to fully explore the use of adlay starch in novel drug delivery systems and pharmaceutical excipients.

Dietary fiber

Tensiska et al. (2015) investigated the dietary fiber content in adlay, reporting values of 12.533 ± 0.07%, 11.982 ± 0.03%, and 9.945 ± 0.14% for whole seeds, seeds with aleurone, and polished seeds, respectively. Dietary fiber is widely recognized for the physiological benefits, including regulating bowel function, increasing stool bulk, and maintaining postprandial blood glucose stability.

Tang et al. (2023) specifically analyzed modified adlay bran for its hypoglycemic activity. The results showed that the dietary fiber content of adlay bran was 24.31±0.08 g/100 g, 17.93±0.04 g/100 g, and 8.44±0.09 g/100 g for cellulose, hemicellulose, and lignin. Furthermore, the monosaccharide composition of soluble dietary fiber was quantified (g/100 g) as follows mannose (3.36±0.03), rhamnose (1.56±0.01), glucose (16.29±0.14), galactose (6.21±0.03), xylose (0.75±0.01), arabinose (1.17), and fucose (0.33±0.01). Tang et al. reported that adlay bran, particularly rich in insoluble fiber, enhanced the nutritional value, and fiber modification improved physicochemical properties. However, studies exploring the use of adlay-derived cellulose in nutraceutical formulations remain scarce.

Cellulose sourced from various natural materials has been extensively used in pharmaceutical and nutraceutical products. For example, SEPPIC has developed cellulose-based excipients that are incorporated into nutraceutical formulations (SEPPIC, 2024). Additionally, various cellulose derivatives, such as carboxymethylcellulose (CMC) and hydroxypropylmethylcellulose (HPMC), are widely used as pharmaceutical excipients due to their functional versatility in controlled-release drug formulations, stabilizers, and thickening agents. This suggests that adlay-derived cellulose can be further explored and modified to enhance the functionality and applicability in nutraceutical formulations. Further structural modification of adlay fiber, such as chemical, enzymatic, or physical processing, can optimize the physicochemical properties for better absorption, bioavailability, and formulation stability.

Arabinoxylan

Arabinoxylans (AX) are non-starch polysaccharides widely reported in grains such as wheat, rye, barley, oats, rice, sorghum, corn, and millet (Erum et al., 2015). Adlay has also been identified as a source of arabinoxylans (Zhu, 2017), presenting an opportunity for further exploration of pharmaceutical and nutraceutical applications.

One of the key functional properties of arabinoxylan is the ability to swell in solvents, forming highly viscous solutions and gels in the presence of oxidizing agents. These characteristics have driven interest in using arabinoxylan as a pharmaceutical excipient, with applications as a drug delivery matrix, suspending agent, emulsifier, foam stabilizer, binder, and disintegrant (Erum et al., 2015).

Erum et al. (2015) reported that arabinoxylan showed antimicrobial activity, although the property was highly dependent on the natural source. This suggests that further validation is required to confirm the broad-spectrum antimicrobial potential, capable of enhancing the application as a multifunctional excipient. Arabinoxylan can also be modified to enhance its functional characteristics, thereby expanding the pharmaceutical use.

Hanif & Zaman (2017) investigated the use of thiolated arabinoxylan in mucoadhesive oral films for delayed drug release. The results showed that oral films had superior mechanical properties and mucoadhesive strength, with a folding resistance exceeding 300 cycles, ensuring structural integrity. The films showed a mucoadhesive strength of 11.53 ± 0.17 N, showing effective adhesion to mucosal surfaces. Moreover, in vitro dissolution and ex vivo permeation studies conducted over an 8-hour period showed sustained drug retention, with 85.03% cumulative release and 78.90% absorption.

Pérez-Flores et al. (2024) conducted a bibliometric analysis on the efficacy of arabinoxylan as a drug delivery vehicle. The results showed that both native and modified arabinoxylan had promising capabilities as a controlled-release platform for biomolecules and

pharmaceuticals. This showed the application of arabinoxylan in various dosage forms, including macrogels such as films, tablets, and hard gelatin capsules; and multi-particle systems such as microgels and nanogels.

Arianty et al. (2024) confirmed the prebiotic activity of arabinoxylan, providing gut health benefits by promoting the growth of beneficial microbiota. This suggests that arabinoxylan in adlay can serve a dual role in nutraceutical formulations, namely as an active biofunctional compound and pharmaceutical excipient in nutraceutical product development. Due to the broad functionality in drug delivery, prebiotic activity, and pharmaceutical formulations, adlay-derived arabinoxylan presents significant potential for further exploration and formulation optimization in nutraceutical and pharmaceutical sciences.

Fructooligosaccharide

Fructooligosaccharide (FOS) is an oligosaccharide characterized by the structural formula GFn, where n fructose molecules are attached to a single glucose residue through a β-(1→2) glycosidic bond at the non-reducing end (Kumar et al., 2018). Additionally, FOS is resistant to enzymatic digestion within the gastrointestinal tract, a property that classifies it as an indigestible oligosaccharide. This property enables FOS to function as a prebiotic, stimulating the growth and proliferation of beneficial gut microbiota.

Beyond the prebiotic role, FOS can bind with other sugars, including fructose, glucose, and sucrose, even when present in low concentrations. This oligosaccharide exists in varying degrees of polymerization, typically comprising 3 to 20 fructose molecules linked through β(2→1) or β(2→6) glycosidic bonds, based on the synthesis method (Alatorre-Santamaría et al., 2022).

FOS is widely recognized for its multifaceted health benefits, including enhancement of immune system function, promotion of beneficial gut microbiota, optimization of digestive processes, alleviation of metabolic syndrome and inflammatory diseases, potential protection against infections and cancer. Due to the unique physicochemical properties, FOS is often used as an additive or matrix component in various food formulations, where it contributes to improving texture, sensory attributes, and mouthfeel. Moreover, FOS is applied in pharmaceutical and cosmetic formulations, expanding beyond the nutraceutical sector.

Basholli-Salihu et al. (2019) investigated the application of prebiotics like FOS as cryoprotectant excipients to enhance the stability and functionality of *Bifidobacterium longum* ssp. infantis, showing the potential for symbiotic applications in food and medicine. During the investigation, freeze-dried *B. longum* ssp. infantis powder was coated with FOS and other sugars. The results showed that cell protection using cellobiose and FOS was superior to sucrose and trehalose. Due to the prebiotic properties and functional versatility, FOS content in adlay presents a promising avenue for further development in nutraceutical formulations, with potential pharmaceutical application as a stabilizing excipient in probiotic-based formulations or as bioactive.

Coixan

Coixan is a distinct polysaccharide found in adlay, showing varied monosaccharide compositions depending on type. Specifically, Coixan A comprises arabinose, mannose, rhamnose, xylose, and galactose in a 1:11:1:1:10 ratio. Coixan B consists of xylose, rhamnose, mannose, galactose, glucose, and arabinose in a 13:3:3:10:5:18 ratio. Meanwhile, Coixan C is classified as a dextran-like polysaccharide (Takahashi et al., 1986; Weng et al., 2022; Yu et al., 2017).

Despite the potential pharmaceutical and nutraceutical applications, there is limited information on the use of coixan as an additive in formulations. Several studies have shown coixan's bioactive properties, suggesting the relevance in nutraceutical development (Igbokwe et al., 2021; Sui & Xu, 2022; Zhu, 2017). A significant investigation into the role of coixan as an excipient was conducted by Qu et al. (2017), who developed a microemulsion system (Gal(oct)-C-MEs) modified with octanoyl galactose ester and self-assembled using coix seed-derived components. The innovative system showed enhanced tumor accumulation through asialoglycoprotein receptor-mediated endocytosis, alongside improved antitumor efficacy by the synergistic effects of multiple bioactive components. These results suggest the potential of coixan as both a bioactive ingredient and a functional excipient, requiring further exploration for nutraceutical and pharmaceutical formulations.

Protein and Lipid

One of the distinctive characteristics of adlay compared to other grains is high protein content,

which ranges from 10% to 20%. According to Chakraborty & Dhar (2017), protein is a promising biomolecule for nano-carrier systems characterized by low cytotoxicity, biocompatibility, and biodegradability. During the study, Liao et al. (2022) investigated the potential of whey protein isolate (WPI), soy protein isolate (SPI), and sodium caseinate (CS) as excipients to enhance the bioaccessibility, water solubility, and chemical stability of quercetin in vitro. The results showed that protein-based matrices could serve as effective carriers for nutraceuticals.

In addition to proteins, lipids, and oils derived from adlay also showed significant potential for nutraceutical applications, as bioactive components or excipients. Lipids play a crucial role in lipid-based drug delivery systems (LBDDS), facilitating the dissolution and stabilization of hydrophobic drugs. According to Nakmode et al. (2022), monoglycerides and diglycerides serve as co-emulsifiers in LBDDS. The primary fatty acids found in adlay seeds are unsaturated fatty acids, including oleic (38–51%), palmitic (14–18%), stearic (2–3%), and linoleic (30–38%) (Zhu, 2017). These previous studies also support the application of adlay oil in both drug delivery systems and bioactive formulations to cancer treatment.

Among the various bioactive components of adlay, seed oil has been the most extensively studied, particularly in pharmaceutical formulations. A significant example is Kanglaite, an herbal medicine derived from adlay seed oil, which has been widely used as an adjuvant treatment for cancer in China. Kanglaite is available in both injectable and capsule formulations, with the potential to enhance quality of life, improve treatment response rates, modulate immune function, and reduce chemotherapy-associated side effects (Lu et al., 2022). A Cochrane database search using the keyword "Coix" identified 10 clinical trials out of 30 relevant studies investigating the use of adlay, either alone or in combination with other herbal compounds, for cancer treatment (Cochrane Central Register of Controlled Trials (CENTRAL), 2018; Hailang et al., 2020). Consequently, studies on adlay-based formulations have been predominantly focused on anticancer applications.

Other Compounds

Among adlay bioactives are policosanols (docosanol, tetracosanol, hexacosanol, and octacosanol), Triterpenes (predominantly found in adlay seeds, including coixan and coixenolide), Phytosterols (squalene, campesterol, tocopherol, ergosterol, and β-sitosterol), and Polyphenols (coniferyl alcohol, syringic acid, ferulic acid, syringaresinol, 4-ketopinoresinol, and p-hydroxybenzaldehyde). Other compounds include flavonoids (apigenin, luteolin, quercetin, kaempferol, naringenin, nobiletin, tangeretin, isoliquiritigenin, eriodictyol, formononetin, and rutin), and other bioactive compounds, including lignans, neolignans, spiroenones, lactams, and spirolactams (Devaraj et al., 2020).

ADLAY PHARMACOLOGICAL ACTIVITIES

Adlay has been empirically used in traditional medicine for its antioxidant, anti-inflammatory, anticancer, antitumor, hypoglycemic, and analgesic activities (Huda et al., 2023; Weng et al., 2022). The traditional medicinal use has persisted longer than as a food source. China remains one of the countries that has preserved the cultural and medicinal applications of adlay because of the belief to confer significant health benefits in traditional formulations. This is shown in the classical text *Shennong Materia Medica Classic*, where adlay seeds are categorized as a top-tier medicinal compound due to sweet taste and slightly cooling nature in Traditional Chinese Medicine (TCM) (Li et al., 2024).

Archaeological investigations at Qiaotou (9000–8700 cal. BP) identified earthen mounds containing pottery jars, which were analyzed and found to contain beer brewed from rice, adlay, and other ingredients. Additionally, in the Tang Dynasty, the text *Prescriptions Worth a Thousand Gold* (*Qian Jin Yao Fang*), compiled by Sun Simiao, described the use of reed stalk soup combined with adlay seeds, reed stalks, winter melon seeds, and other ingredients for the treatment of pulmonary abscesses, pneumonia, and bronchitis (Li et al., 2024).

The traditional use of adlay in herbal medicine provides empirical evidence suggesting its pharmacological effects. This has prompted extensive study to investigate the biological activities. Recent studies have reported various pharmacological properties of adlay, including anticancer, anti-obesity, hypoglycemic, immunomodulatory, and gut microbiota regulatory effects, among others (Huda et al., 2023; Li et al., 2024; Weng et al., 2022). The following presents recent studies (2019–present) on the pharmacological activities of adlay.

Anti-cancer

Among the various pharmacological activities investigated in adlay, the anticancer activity has been the most extensively studied. This is due to the empirical use in traditional medicine for cancer treatment, particularly as an adjuvant treatment (Zhang et al., 2020). Previous studies also validated the anticancer potential of adlay through in vitro analysis, showing the efficacy against various cancer cell lines. These included hepatoma (HepG2), gastric carcinoma (SGC-7901), cervical cancer (HeLa), colon cancer (HT-29, HCT116, and CCD-18Co), breast cancer (MCF-7), lung adenocarcinoma, human uterine sarcoma (MES-SA), and multidrug-resistant human uterine sarcoma (MES-SA/Dx5), among others (Chang et al., 2018; Chiang et al., 2022; Meng et al., 2023; Ni et al., 2021; Son et al., 2017; Son et al., 2019; Yu et al., 2021).

Liu et al. (2019) investigated the effects of adlay seed oil on cancer cachexia using an in vivo model with C57BL/6 mice bearing Lewis lung carcinoma. The results showed that adlay seed oil prevented cachexia and ameliorated systemic inflammation without affecting food intake or tumor size. This effect was mediated through the downregulation of Muscle Ring Finger-1 (MuRF1) expression and a decreased phospho-p65 (Ser536) to p65 ratio in muscle tissue, as well as the inhibition of hormone-sensitive triglyceride lipase (HSL) activation and AMP-activated protein kinase (AMPK) signaling. Zhang et al. (2019) conducted a clinical study evaluating the effects of adlay seed oil injection for cancer pain management. The results showed that adlay seed oil injection effectively reduced pain levels in cancer patients and improved quality of life, without significant adverse effects.

Fang et al. (2020) investigated adlay seed oil both in vitro and in vivo to evaluate the efficacy against triple-negative breast cancer (TNBC). The study provided positive evidence supporting the potential role of adlay seed oil in TNBC treatment through modulation of the miR-205/S1PR1 signaling axis. In addition to oil, adlay seed extract was investigated for its effects on lung adenocarcinoma (LUAD) in vitro (Jiang et al., 2024). The result showed that the extract inhibited the malignant progression of lung adenocarcinoma through modification of TOP2A ubiquitination mediated by KCTD9.

Qian et al. (2019) explored adlay seed extract as an adjuvant treatment for pancreatic cancer in combination with gemcitabine, using both in vivo and in vitro models. The results showed that adlay seed extract had synergistic effects with gemcitabine, further supporting the potential in pancreatic cancer treatment. Additionally, fractions and subfractions of ethanolic adlay seed extract were shown to induce cell cycle arrest and apoptosis in breast cancer (MCF-7) and cervical cancer (HeLa) cell lines.

The studies support the anticancer potential of adlay, showing single treatment effects and synergistic properties in combination with conventional chemotherapy. Furthermore, a systematic review and meta-analysis showed that adlay, particularly the seeds, was both effective and safe as an adjunctive treatment for certain types of cancer (Lu et al., 2022).

Anti-obesity

Shin et al. (2024) conducted an in vivo study to evaluate the effects of adlay seed supplementation on metabolic health and gut microbiota in mice subjected to a high-fat diet (HFD). Liu et al. (2019) specifically showed the role of gut microbiota in obesity and provided empirical evidence supporting this association. The results showed that seed supplementation promoted the growth of beneficial bacteria genera, including Lactobacillus, Coprococcus, and Akkermansia, as well as specific species such as *Akkermansia muciniphila* and *Lactobacillus agilis*. These bacteria populations are associated with obesity reduction, high glucose tolerance, and decreased total cholesterol and fat mass. Furthermore, the seed supplementation was observed to function as a prebiotic, contributing to weight loss and preventing metabolic disorders related to obesity.

Another study by Shin et al. (2024) confirmed the anti-obesity effects of adlay sprouts, tested in vitro using Huh7 hepatocyte cells and in vivo in C57BL/6J mice. In vitro, Huh7 cells were induced with free fatty acids and treated with adlay sprout extract. Meanwhile, in vivo, mice were fed a 60% HFD and administered 200 mg/kg/day of adlay sprout extract. The results showed a significant reduction in intracellular triglyceride (TG) accumulation, downregulation of lipogenesis-related genes (Pparγ, Srebp1c, and mutant Pnpla3), and upregulation of the lipolytic enzyme ATGL in vitro. Specifically, in vivo results further supported these effects, showing dose-dependent reductions in body weight gain, epididymal fat mass, and serum lipid biomarkers. Adlay sprout supplementation was also observed to improve hepatic and adipose tissue histology, supporting

the potential as an anti-obesity nutraceutical for weight management.

Zhang et al. (2023) explored the synergistic effects of adlay seed extract in combination with the probiotic *Lactobacillus paracasei* K56 in an in vivo obesity model. The results showed that adlay seed extract combined with *L. paracasei* K56 effectively reduced body weight, epididymal fat, and perirenal fat mass. The combination improved fasting blood glucose levels, lipid profiles (increasing HDL while reducing VLDL), inflammatory markers, and hepatic lipid synthesis enzymes, showing thepotential in obesity management.

Huang et al. (2021) previously investigated the anti-obesity effects of adlay bran extract obtained through supercritical extraction in an in vivo hamster model. In this study, hamsters were subjected to an HFD and treated with varying doses of adlay bran extract. The results showed a significant reduction in weight gain, triglyceride levels, total cholesterol, and LDL cholesterol, alongside an increase in HDL cholesterol. Moreover, adlay bran extract enhanced cholesterol metabolism and bile acid excretion, further showing the beneficial effects on lipid regulation. These lipid-modulating effects were attributed to the high content of linoleic acid (28.59%), oleic acid (56.95%), and bioactive compounds such as β-sitosterol (4117.72 ppm) and feruloyl-β-sitostanol derivatives.

Chen et al. (2022) investigated the effects of adlay seed oil in an obesity-induced mouse model. In line with previous studies, adlay seed oil showed significant weight-reducing effects, decreasing body weight, liver weight, total cholesterol, and triglyceride levels. Furthermore, adlay seed oil ameliorated hepatic lipid deposition and metabolic disturbances induced by excessive dietary fat intake. These effects were attributed to the presence of unsaturated fatty acids in adlay seed oil, which contributed to its lipid-lowering and metabolic regulatory properties.

Immunomodulator and anti-inflammatory activity

Beyond the anti-obesity properties, Lee et al. (2024) explored the anti-pruritic and immunomodulatory effects of adlay sprout extract using in vivo and in vitro models, specifically in HMC-1 mast cells (a primary cell line model). The results showed that adlay sprout extract effectively inhibited histamine release and IL-31 production, a key pro-inflammatory cytokine, surpassing the positive control group treated with prednisolone. Furthermore, the extract significantly suppressed mast cell proliferation, tryptase expression, nitric oxide (NO) production, and other inflammatory mediators. This is due to the anti-inflammatory and immunomodulatory effects of coixol, a bioactive compound found in adlay sprouts.

The immunomodulatory effects of adlay seeds have been explored, particularly in the treatment of colitis. An in vivo study on a colitis-induced rat model showed that adlay seed consumption alleviated colitis symptoms, reduced inflammatory cytokine secretion, and mitigated oxidative stress. These effects were related to the modulation of T-cell regulation, as observed in colon tissue analysis (Zhou et al., 2022).

Fermented adlay seed polysaccharides were reported to maintain immune homeostasis by regulating the Th1/Th2 cytokine balance in vivo (Wang et al., 2022). Further studies also confirmed the anti-inflammatory potential of adlay seed polysaccharides, as shown by both in vitro and in vivo investigations (Sui & Xu, 2022). These results collectively underscore the treatment potential of adlay as an immunomodulatory and anti-inflammatory agent, further expanding the applications beyond metabolic health.

Other pharmacological activities

Huang et al. (2021) conducted a study exploring the lipid-regulating potential of supercritical fluid extract from adlay bran (AB-SCF) and identified the bioactive components. AB-SCF was administered at various doses (30.84–616.70 mg/kg body weight) to hyperlipidemic hamsters induced by a high-fat diet (HFD) for eight weeks. The treatment significantly reduced body weight gain, serum triglycerides (TG), total cholesterol (TC), and LDL-C levels. Meanwhile, HDL-C levels were increased, causing a reduction in cardiovascular risk and improving hepatic lipid profiles. AB-SCF enhanced cholesterol metabolism and bile acid excretion, showing benefits for lipid homeostasis. Mechanistic studies showed that AB-SCF upregulated lipoprotein lipase (LPL), AMPK, and phosphorylated AMPK (p-AMPK), while downregulating fatty acid synthase (FAS), thereby supporting the role in alleviating hyperlipidemia (Huang et al., 2021).

A separate study investigated the effects of adlay seed oil on obesity and lipid metabolism in HFD-induced obese mice (Chen et al., 2022). The results showed that adlay seed oil significantly reduced body weight, liver weight, total

cholesterol, and triglyceride levels compared to other dietary fats. Furthermore, the oil ameliorated hepatic lipid accumulation and metabolic disturbances induced by excessive fat intake. Gas chromatography analysis showed that supercritical fluid-extracted adlay seed oil was rich in medium-chain fatty acids (MCFAs), particularly capric acid (35.28%) and lauric acid (22.21%), which contributed to the lipid-regulating properties. These characteristics allow adlay seed oil to modulate hepatic fatty acid metabolism and lipid levels effectively. Additionally, Chen et al. identified adlay seed oil as a promising functional lipid with potential as a healthier alternative to conventional dietary fats for the prevention of metabolic disorders.

ADLAY APPLICATIONS: ENHANCING THE NUTRITION

Adlay has been consumed as a food source across various regions globally. However, compared to its cereal counterpart, like maize, adlay has received less attention as a staple food. Historical records show that adlay was once a primary staple in Bhutan before being replaced by maize due to higher popularity and agronomic advantages. In Indonesia, adlay was traditionally used as a hedge plant and remained relatively underutilized. Certain regions in the country have been familiar with adlay consumption, including Agam District (*Canduang, Sungai Pua, Banuhampu*), Padang Pariaman District (*Batang Anai*), and Padang City (*Pauh*). Furthermore, West Javanese communities incorporate this cereal into various traditional foods, such as porridge, dodol (glutinous sweets), and assorted cakes (Nurmala, 2011; Ramadhan et al., 2024).

The concept of functional foods has gained significant attention in modern nutrition and pharmaceutical sciences. According to Health Canada, functional foods are defined as "conventional or foods resembling conventional foods, which form part of a daily diet. These functional foods have been shown to provide health benefits or reduce the risk of specific chronic diseases beyond basic nutritional functions" (Sreerag & Balakrishnan, 2022). Similarly, the Indonesian Food and Drug Authority (*Badan Pengawas Obat dan Makanan, BPOM*) defines functional foods as "processed foods containing one or more components with scientifically proven physiological benefits beyond basic nutritional functions, ensuring safety and providing health advantages" (BPOM RI, 2011).

Functional foods can be classified into several categories, including enriched (nutrient-enhanced), fortified, altered (modified), and enhanced products. Additionally, some definitions include naturally occurring, unprocessed foods with inherent health benefits as part of the functional food spectrum. Due to the bioactive compounds and pharmacological potential, adlay holds strong promise as a functional food candidate for both nutritional and therapeutic applications.

In addition to the use in snack formulations, the sensory and physicochemical evaluation of adlay-based functional foods has been investigated in several studies. Yusuf et al. (2022) examined the physical modification of adlay through pregelatinization using an autoclave for the development of instant porridge. The results showed that pregelatinization enhanced water absorption, solubility, and swelling power, while also modifying pasting properties, reducing flour particle weight, and increasing consumer acceptability. However, nutritional parameters were not included in the study. Duan et al. (2024) investigated the effects of extrusion processing on instant porridge, showing that extrusion reduced viscosity and improved stability. At a moisture content of 18–22%, the extrusion process did not affect soluble protein content but decreased the starch digestibility ratio, thereby enhancing the nutritional profile of the porridge.

The formulation of adlay-based functional foods has been explored in cookies. Specifically, Iwansyah et al. (2022) developed a cookie formulation combining adlay and moringa, while Shen et al. (2024) formulated cookies incorporating adlay, *Gastrodia elata Bl.*, black sesame seeds (*Sesamum indicum L.*), walnuts (*Juglans regia L.*), jujube (*Ziziphus jujuba Mill.*), and *Poria cocos*. The study by Iwansyah et al. showed that the cookies were nutrient-dense, safe for consumption, and well-accepted in sensory evaluation. Therefore, cookies were recommended for individuals requiring high-energy snacks.

Compared to Iwansyah et al., who studied sensory and nutritional evaluation, Shen et al. (2024) investigated the functional health effects of medicinal food-formulated biscuits on intestinal mucosal microbiota, brain function, and antioxidant activity in mice. The results showed that consumption of these functional biscuits influenced gut microbiota diversity, increased hippocampal norepinephrine (NE) levels across all dose ranges, reduced hepatic malondialdehyde (MDA) levels, and enhanced hippocampal choline

acetyltransferase (ChT) activity at medium and high doses. Additionally, a correlation was identified between gut microbiota composition and NE, ChT, and MDA levels, further supporting the neuroprotective and metabolic regulatory potential of adlay-based functional foods. The study by Shen et al. provided compelling evidence for the health-promoting properties of adlay-based functional foods and the potential applications in cognitive health and metabolic regulation.

Rao et al. (2023) and Sanjaya & Romulo (2023) investigated the application of adlay in beverage formulations, each focusing on different product concepts. Specifically, Rao et al. (2023) formulated a hydrothermally and enzymatically processed adlay-based beverage combined with chrysanthemum and evaluated the anti-inflammatory effects through in silico analysis. The results showed that the chrysanthemum-adlay beverage had a higher concentration of crude polysaccharides and reducing sugars, a harmonious aroma profile characterized through HS-SPME-GC/MS analysis, and significant anti-inflammatory properties.

Sanjaya & Romulo (2023) developed a functional beverage combining adlay with sorghum. The formulation caused a significant increase in carbohydrate content, rising from 1.24% to 2.71%, along with a slight improvement in protein content from 0.27% to 0.33%. Additionally, the moisture content decreased from 98.47% to 96.91%, accompanied by a significant reduction in sodium and potassium levels. However, it was observed that higher concentrations of adlay negatively impacted the physical stability of the product and reduced sensory appeal.

ADLAY APPLICATION: PHARMACEUTICAL PROSPECTS

Studies on adlay formulations have predominantly focused on microemulsion systems, with 10 publications indexed in Scopus (Scopus, 2024). Liposomal formulations have been reported in two studies (Bai et al., 2011, 2019), while nanostructured lipid carriers (NLCs) have been investigated in one study (Zhu et al., 2020). However, there is no documented report on conventional dosage forms such as tablets or capsules. There are also no studies on the nutraceutical activity of adlay within pharmaceutical formulations, although the bioactive constituents of adlay require further investigation for potential therapeutic applications.

The most studied formulation using adlay is a microemulsion for cancer treatment. One of the significant anticancer formulation studies, including adlay, was conducted by Xiao et al. (2019), who developed adlay seed oil microemulsion using EL-40/Span 80/ethanol/adlay seed oil, with an optimized EL-40/Span 80 ratio of 5:1 (w/w) and a surfactant-to-cosurfactant weight ratio (Km) of 3:1. The resulting spherical droplets (36.2 nm) showed enhanced stability compared to unformulated adlay oil. In vivo studies showed sustained drug release and high bioavailability, with preferential distribution in the liver, lungs, and kidneys.

Another study conducted by Chen et al. (2018) focused on the development of a transferrin-modified microemulsion system containing adlay seed oil and tripterin for cervical cancer treatment. The results showed that transferrin-modified microemulsions had 2.58-fold greater cytotoxicity against HeLa cells and higher apoptosis rates compared to conventional microemulsions or tripterin alone. Chen et al. (2023) also explored a paclitaxel-adlay seed oil microemulsion formulation to enhance the solubility and anticancer efficacy of paclitaxel. In this system, adlay seed oil served primarily as the oil phase, replacing conventional organic solvents. The microemulsion was formulated using a self-emulsifying method, with an HS 15:PEG 400 combination, leading to a clear, transparent microemulsion with a particle size of 30.28 ± 0.36 nm and a slightly negative surface charge (-4.40 ± 1.13 mV). The formulation achieved a 98% encapsulation efficiency, showing a cumulative drug release of 80.21% over 48 hours. Moreover, the apoptosis rate of cancer cells treated with this formulation was 1.7 times higher than that of paclitaxel alone.

Advancing the adlay-based formulations, Chen et al. (2024) developed a multicomponent system for liver cancer treatment, incorporating adlay seed oil-based celastrol microemulsions into tetrandrine-loaded liposomes through the thin-film dispersion method. The result showed that encapsulation of celastrol-adlay seed oil microemulsions within tetrandrine liposomes resulted in superior tumor targeting and biodistribution compared to single-component systems. These advancements in adlay oil-based microemulsions and liposomal formulations underscore the potential of adlay seed oil in anticancer drug delivery.

Encapsulation of β-carotene and adlay seed oil in liposomes has been shown to enhance anticancer activity, antioxidant potential, and bioavailability (Bai et al., 2019). Additionally, another liposomal system was developed using the supercritical fluid (SCF) carbon dioxide method with sonication to encapsulate adlay extract fraction for colorectal cancer treatment (Sainakham et al., 2016). The encapsulated adlay extract showed greater stability and superior in vivo tumor suppression compared to its non-encapsulated counterpart.

Liposomal formulations of adlay remain less explored compared to microemulsions. Furthermore, studies focusing on anticancer activity in adlay-based formulations have predominantly investigated adlay oil due to its established role as an adjuvant therapy for chemotherapy. However, unformulated bioactive components of adlay, including other plant fractions, also show promising anticancer potential. This shows the untapped opportunities for adlay in the development of nutraceuticals as adjuncts for cancer treatment.

SAFETY OF ADLAY

Hayashi, Ohta, et al. (2009) conducted an acute oral toxicity test in mice using various parts of adlay seeds extracted with hot water. The whole-seed extract of adlay showed excellent safety, with a lethal dose (LD_{50}) exceeding 2000 mg/kg. Furthermore, Hayashi, Arai, et al. (2009) performed a 28-day repeated oral toxicity study (sub-acute toxicity) using the same sample, confirming that the aqueous extract of whole adlay seeds was safe, with an LD_{50} also exceeding 2000 mg/kg.

Kim et al. (2021) conducted a single-dose oral toxicity test in Sprague-Dawley mice, showing that adlay sprouts had an LD_{50} > 5000 mg/kg. Furthermore, no significant toxicity or abnormalities were observed in experimental rats regarding body weight, urinalysis, or haematological and histopathological examinations (Igbokwe et al., 2021). Burnett et al. (2017) previously reported the safety of various plant-based oils, including adlay seed oil.

Beyond toxicity assessments, mycotoxin contamination, particularly aflatoxin B1, due to fungal infestation during postharvest processing and storage, remains a critical concern for adlay (Huda et al., 2023). To mitigate this risk, implementing postharvest protocols such as heated-air drying, early dehulling, and reducing storage duration can effectively limit mycotoxin levels in consumable products (Choi et al., 2014).

From the perspective of Traditional Chinese Medicine (TCM), coix seeds are recommended to be roasted before consumption, particularly for individuals suffering from diarrhea and spleen deficiency. Furthermore, based on the yin-yang balance, coix seeds should be consumed cautiously by individuals with fluid deficiency post-fever or those who are naturally yin-deficient. Pregnant women and individuals with constipation are advised to avoid consuming adlay (Meng et al., 2023).

FUTURE PROSPECTS OF ADLAY IN NUTRACEUTICAL FORMULATION

Among the various bioactive components of adlay, seed oil has gained significant attention due to its crucial role in cancer adjuvant treatment in China. The nutraceutical potential of adlay, particularly the synergistic effects in cancer treatment, remains an area for further investigation, presenting new opportunities for oncology treatment. In addition to the lipid constituents, other phytochemicals such as fatty acids, esters, polysaccharides, sterols, alkaloids, triterpenes, tocopherols, lactams, lignans, phenols, flavonoids, and related compounds have shown various pharmacological activities. These include hepatoprotective effects, gut microbiota modulation, splenic function enhancement, and anti-inflammatory properties (Li et al., 2024).

Adlay shows significant functional advantages in pharmaceutical formulations. However, most formulation-based studies have been predominantly focused on seed oil, rather than other bioactive constituents. Studies on adlay oil have increased the dual role as a bioactive agent and co-drug in anticancer drug formulations, supporting the promising potential as a nutraceutical adjunct in cancer treatment. Despite the increasing number of studies on adlay oil-based formulations, there is limited information on the formulation and quality evaluation of other adlay-derived bioactives. Therefore, further exploration of non-oil adlay components, including their formulation stability, pharmacokinetics, and therapeutic efficacy, represents an untapped opportunity for the development of adlay-based pharmaceutical and nutraceutical applications.

CONCLUSION

In conclusion, this review shows that adlay has been traditionally used for various purposes,

including food ingredients and as a part of medicinal practice. However, the widespread application remains limited because adlay is mainly cultivated as a hedge plant. In China, this cereal is incorporated into traditional medicinal prescriptions and consumed as food like porridge. Several studies have attempted to enhance the value of adlay by exploring its potential as a functional food, showing that the combination with other ingredients can improve the nutritional profile of the final product. Building on these results, adlay shows promising potential for development as a nutraceutical product, which can further increase the quality and economic value.

The health benefits of adlay, as elaborated in this review, include the hypoglycemic, hypolipidemic, immunomodulatory, and prebiotic properties, as well as the potential role in adjunct cancer therapy. In pharmaceutical applications, adlay has been explored primarily in formulation studies, with a predominant focus on seed oil. The most extensively explored formulations include adlay in microemulsions, liposomes, and NLCs for cancer treatment.

Regarding safety, existing studies show that adlay is well-tolerated. Therefore, there is an opportunity for further exploration of other parts of the plant and the potential pharmaceutical applications, particularly in nutraceutical product development.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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