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Review Article

Update review: Etnopharmacological, bioactivity and phytochemical of *Allium cepa* L.

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Abstract

Allium cepa L. is commonly used as a vegetable, spice, and in traditional medicine. In traditional medicine, *A. cepa* is applied based on its long-standing usage. This plant has been reported to have therapeutic effects on various conditions, including diabetes, various types of cancer, cough, influenza, dermatological problems, diarrhea, menstrual and abdominal pain, and malaria. Phytochemical analysis of *A. cepa* has identified polyphenols, flavonoids, steroid saponins, furostanol saponins, and sulfur compounds, which are believed to be responsible for its bioactivities. These bioactivities include antioxidant properties, which are associated with other activities such as anti-aging, antidiabetic, and anticancer effects. Additionally, *A. cepa* exhibits antimicrobial and antiplatelet activities.

Keywords

Onion, antioxidant, traditional medicine

Introduction

Allium cepa L. is a member of the Liliaceae family and has been cultivated worldwide as a vegetable (Benitez et al. 2011). Apart from its use as a vegetable, *A. cepa* is commonly used as an ingredient in various cuisines, particularly in Indonesia. The addition of *A. cepa* bulb enhances the flavor of many Indonesian dishes, such as curry, rendang, satay, spicy and sour foods, and others. Furthermore, *A. cepa* has a long history of traditional use in the treatment of diseases such as diarrhea, promotion of blood flow, diabetes, and stomach ailments in several countries, including Indonesia, Africa, China, and India. The traditional medicinal use of *A. cepa* has garnered significant interest among researchers, leading to numerous studies on the phytochemical composition of this plant. Previous research has identified flavonoids, phenolic compounds, and organosulfur compounds as contributors to its traditional medicinal properties. This article provides an updated review on the traditional medicinal use of *A. cepa*, its phytochemical composition, and studies on its bioactivity.

Materials and method

This study utilized research or original articles published between 2011 and 2022. The search was conducted using databases such as Science Direct and PubMed, with a requirement that articles be written in English. Exclusion criteria were applied to articles with the keyword *A. cepa* that were not related to ethnobotanical, ethnopharmacological, phytochemical evaluation, and bioactivity. The scope of this review is focused on the traditional medicinal use, bioactivity, and bioactive compounds of *A. cepa*.

PENSOFT.

Traditional medicinal use

Throughout history, both humans and plants have played a significant role in the treatment of diseases, establishing a strong bond between humans and the plant kingdom (Basu et al. 2014). Among the diverse array of medicinal plants, *A. cepa* stands out not only as a spice used to enhance the taste of food but also as an herbal medicine. *A. cepa* has been employed as a traditional medicine for centuries worldwide. Through a literature review conducted for this study, we aim to gain insights into the historical and contemporary uses of *A. cepa* in different cultures across the globe.

The data from Table 1 indicates that the bulb of *A. cepa* is widely utilized as a traditional medicine. The bulb of *A. cepa* is commonly employed for the treatment of various conditions, including diabetes, different types of cancer, influenza, cough, allergies, and dermatological problems. Additionally, it is frequently used to alleviate pain, such as menstrual and abdominal pain, as well as for treating malaria, diarrhea, and hypertension.

Phytochemical composition of *A. cepa*

The bulbs of *A. cepa* are recognized for their rich content of secondary metabolites, such as flavonoids, polyphenols, and steroids/triterpenoids. A summary of the phytochemical constituents of *A. cepa* is presented in Table 2.

The bioactivity of *A. cepa*

Antioxidant activity

Antioxidants are natural or chemical compounds that can prevent oxidative stress and scavenge free radicals. Oxidative stress arises from an imbalance between free radicals and antioxidants in our bodies (Islam 2006). While our bodies can produce natural antioxidants, they may not be sufficient to inactivate all free radicals. Therefore, additional antioxidants from external sources, such as plants

Table 1. The utilization of *Allium cepa* in traditional medicine globally.

No	Country	Part of the plant	Treatment	How to use	Dose	References
1	Africa	Bulb	Antidiabetic, cataract, erectile dysfunction Renal failure and Hear loss	Decoction Juice and add honey (1 teaspoon)	Drink 1 cup daily for 1 week Drink 1 cup daily for 3 months	Mootoosamy and Mahomoodally 2014
2	Algeria	Bulb	Treat a Stomach, lung cancer	Juice, decoction	n.d.	Taibi et al. 2020
3	China	Seeds	Diarrhea and promote blood flow	n.d.	n.d.	Li et al. 2014
4	France	Bulb	Supplementary traditional folk remedy for cancer treatment	n.d.	n.d.	Han et al. 2013
5	India	Bulb	Menstrual disorders Treatment for skin allergy	Raw, half teaspoon of extract with honey	Early morning for two weeks on an empty stomach	Bhatia et al. 2015
		Bulb	Fever, cold, cough, headache	decoction	50–100 ml taken twice a day till cure	Silambarasan et al. 2017
		Bulb	Antidiabetic	n.d.	n.d.	Thirumalai et al. 2012
6	Indonesia	Bulb	Malaria	Paste for a massage	n.d.	Taek et al. 2019
7	Pakistan	Bulb	Treat abortive disorders, blood sugar control and high blood pressure Treat esophageal cancer	Decoction Paste	n.d. n.d.	Ahmad et al. 2016 Khan et al. 2021
8	Philippine	Leaves	For abdominal pain, antimicrobial and antioxidant	n.d.	n.d.	Clemen-Pascual et al. 2022
9	Saudi Arabia		For respiratory, skin, ear and throat, digestive diseases.	Infusion, decoction, juice	Oral ingestion	Alqethami et al. 2020
10	Serbia	Bulb	Tonic, colds, coughs Injuries, swelling, hematomas, cuts, toothache	Tea and add of honey Raw	about 300 g finely chopped onion is added to ½ kg honey and left overnight it is directly applied	Jarić et al. 2015
11	Spain	Bulb	Treatment of wounds and pimples uses	Poultice with boiled or roasted bulb	n.d.	Cavero et al. 2013
12	Turkey	Bulb	Anti-rheumatic	Infusion	Compress or drink drink one cup of the plant on an empty stomach in the morning	Hayta et al. 2014
13	Yemen	Bulb	Antimalarial	Decoction. Triturated and stirred	One teaspoonful is taken orally once a day until recovery. Paste of leaves and bulb is also applied topically	Al-Adhroey et al. 2020
14	Romania	Bulb	anthelmintic, for cough and hypertension	n.d.	n.d.	Papp et al. 2014
			Common cold or influenza	n.d.	n.d.	Chiru et al. 2020

Table 2. Phytochemicals of *A. cepa*.

Metabolites	Chemical compound	Source	References
Furostanol Saponin	Ceparosides E-L	Ethanol extract	Li et al. 2014
Polyphenol	(1): quercetin 3-glucoside (2): quercetin 4'-glucoside (3): quercetin 3,4'-diglucoside; (4): quercetin 7,4'-diglucoside (5): quercetin 3,7,4'-triglucoside (6): isorhamnetin 4'-glucoside (7): isorhamnetin 4'-galactoside (8): Isorhamnetin 3,4'-diglucoside (9): Iso-quercitrin (10): kaempferol (12): Protocatechuic acid (13) Cyanidin 3 – glucoside, (13): Cepaflavas A – B (14): Cepadials A – D (15): Cepabiflas A – C	PEAL (Polyphenol extracted from lyophilized *A.cepa* L) in butanol solvent	Han et al. 2013; Sato et al. 2015; Li et al. 2020; Celano et al. 2021; Vu et al. 2020
Carbohydrate	Fructo-oligosaccharides (FOS)	Hot 80% ethanol extract	Kumar et al. 2015
Steroid Saponin	Alliospiroside A	80% methanol extract of dry roots	Abdelrahman et al. 2017
Sulfur compound	(1): Allcin, (2): Allyl methyl disulfide, (3): Methyl propyl disulfide, (4): 2,4-Dimethyl thiophene, (5): 1,5-Dithiocan, (6): Dipropyl disulfide	The fresh leaves hydrodistillates	Gitin et al. 2014

and vegetables that are rich in antioxidants, are necessary. *Allium cepa* is one such plant known to possess compounds with antioxidant activity, which has attracted the interest of many researchers.

Commonly used antioxidant testing methods include 2,2'-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS), 2,2-diphenyl-1-picrylhydrazyl (DPPH), Fe^{2+} chelating activity, ferric-reducing antioxidant power assay (FRAP), H2O2 radical scavenging activity, and Trolox equivalent antioxidant activity (TEAC) method. Each method has its own advantages and disadvantages, and the choice of method depends on the study objectives, availability of resources, physical and chemical properties of the samples, sample size, and other relevant factors.

Kumar et al. (2013) reported that the aqueous extract of *A. cepa* exhibited antioxidant potency with an IC_{50} value of 195.2 ± 0.2 µg/mL. Another study by Fredotovic et al. (2017) investigated the methanolic extract of *A. cepa* and reported a DPPH scavenging percentage of 64.82% at a sample concentration of 100 µg/mL. Antioxidant activity was also tested on the essential oil derived from *A. cepa*, with a reported IC_{50} value of 630 µg/mL for DPPH (Ye et al. 2013). Furthermore, the IC_{50} value of total polyphenols in onions for DPPH testing was found to be 43.24 µg/mL (Ouyang et al. 2018).

Essential oils are typically found in nonpolar extracts, while polyphenols are usually present in semi-polar extracts. Previous research has reported that semi-polar to polar solvent extracts exhibited lower IC_{50} values compared to nonpolar solvent extracts.

Sidhu et al. (2019) conducted a study to investigate the antioxidant activity of various layers of *A. cepa* (Egyptian red onion) bulbs, including the outer, middle, and inner layers. The results showed that the outermost layer had the highest concentration of antioxidant compounds compared to the other layers, with a Trolox equivalent antioxidant activity (TEAC) value of 2457.0 mmol/100 g. This may be attributed to the outermost layer being more exposed to external factors such as plant pests and climate changes, which stimulate the production of secondary metabolites in plants.

While the bulb of *A. cepa* is commonly used, the peel of *A. cepa* also has potential as a medicinal component. Although the peel is not typically consumed by humans and is often discarded as waste, Masood et al. (2023) were interested in studying the antioxidant activity of the peel in comparison to the bulb of *A. cepa*. The results showed that the ethanolic extract of the peel exhibited higher antioxidant activity than the ethanolic extract of the bulb, as determined by ABTS, DPPH, FRAP, Fe^{2+} chelating activity, and H2O2 radical scavenging activity. Therefore, it can be concluded that all parts of A. cepa have the potential to serve as a source of antioxidants.

Antioxidant activity is often associated with phenolic compounds, which contain a hydroxyl group (OH) directly bonded to a phenyl group. *A. cepa* is known to contain quercetin, iso-quercitrin, and gallic acid. Correlation analysis between antioxidant activity and total phenolic content (TPC) has shown a statistically positive relationship. Higher TPC values correspond to increased antioxidant activity (Muflihah et al. 2021). Antioxidant activity is also influenced by the flavonoid group. Higher total flavonoid content (TFC) leads to increased antioxidant activity, which can be attributed to the position of the OH groups on the flavonoid structure. The presence of a hydroxyl group at the 3-OH position on ring B, as well as ortho-hydroxy groups on rings A and B, positively affect the activity (Treml and Smejkal 2016; Fitriansyah et al. 2022).

Based on the data presented in Table 2, it appears that the polyphenol compounds responsible for this activity include quercetin 3-glucoside, quercetin 4'-glucoside, quercetin 3,4'-diglucoside, quercetin 7,4'-diglucoside, isorhamnetin 4'-galactoside, quercetin 3,7,4'-triglucoside, isorhamnetin 3,4'-diglucoside, isorhamnetin 4'-glucoside, and iso-quercitrin.

Cytotoxic activity

Erukainure et al. (2021) demonstrated the cytotoxic effects of the ethyl acetate extract of *A. cepa* yellow var. on normal human embryonic kidney cells (HEK293). The GC-MS analysis of the ethyl acetate extract revealed the presence of phytol acetate, pentadecanoic acid, and allyl ionone as the predominant fatty acids, while campesterol, cycloartenol-3β acetate, ergost-7-en-3β-ol, fucosterol, and sitosterol were identified as the predominant sterols.

Anti-hyperglycemic

Diabetes mellitus is a major health problem worldwide. Several researchers have reported an association between phenolic compounds in herbs and plants and their α-glucosidase inhibitory activity and antioxidant activity (Kwon et al. 2006). Diabetes is characterized by hyperglycemia, increased production of free radicals, and predisposition to oxidative stress, leading to diabetes complications (Masood et al. 2023).

Supplementation of bread with 1% and 3% peel extract of *A. cepa* powder and 7% onion has been shown to reduce blood sugar and malondialdehyde (MDA) levels in diabetic rats after eight weeks of treatment. Moreover, *A. cepa* supplementation significantly improved antioxidant enzyme activity in treated diabetic rats (Masood et al. 2021). Another study investigated the α-glucosidase inhibitory activity of the ethanolic extract of *A. cepa* bulbs and peels, which demonstrated a reduction in blood glucose levels by decreasing glucose absorption rate. The ethanolic extract of *A. cepa* peels exhibited 80% inhibition of α-glucosidase activity (Masood et al. 2023).

Anti-obesity

Obesity is defined as a significant increase in body weight or body mass index (BMI) (Novelli et al. 2007; Amin and Nagy 2009). *A. cepa* contains flavonoids and saponins that are associated with a pancreatic lipase inhibitory effect (Marelli et al. 2022). According to the study by Marelli et al. (2022), *A. cepa* inhibits the hydrolysis of lipid esters and exhibits a protective effect against phospholipases through the action of active intermolecular molecules. *A. cepa* also contains secondary metabolites such as squalene, which inhibits cholesterol biosynthesis by inhibiting 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase in the liver (Ibrahim et al. 2020). Administration of 10% and 20% *A. cepa* leaf extracts resulted in decreased levels of triglycerides, total cholesterol, VLDL cholesterol, and LDL cholesterol (Momoh et al. 2022). Li et al. (2020) reported that *A. cepa* extract at a dose of 4.5 g/kg body weight showed potential as an antihyperlipidemic agent. *A. cepa* is rich in quercetin and isoquercitrin, which are known to be responsible for the antihyperlipidemic effect.

Dermatologic problem

Tyrosinase inhibitory activity was tested using L-DOPA or L-tyrosinase, with IC_{50} values of 52.7 μM and 4.3 μM, respectively (Arung et al. 2011a). The study reported that quercetin 4'-O-β-D-glucopyranoside, isolated from the dry skin of *A. cepa*, is responsible for this activity. The results indicate that dried red onion peel contains skin-whitening ingredients with anti-tyrosinase activity. Arung et al. (2011b) also reported that the methanol extract of dry skin from *A. cepa* contains quercetin-3'-O-β-D-glucoside, which can inhibit melanogenesis in B16 melanoma cells with an IC_{50} value of 38.8 μM.

Antimicrobial

Bacterial pathogens, such as *Bacillus cereus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Mycobacterium tuberculosis*, *Pseudomonas aeruginosa*, *Salmonella typimurium*, *Staphylococcus aureus*, and *Streptococcus pneumoniae*, are microorganisms that can cause mild to severe infections and are responsible for numerous deaths (GBD 2019 Antimicrobial Resistance Collaborator 2022). Antibacterial agents are substances that can kill or inhibit the growth of bacterial pathogens, thereby minimizing their pathogenic effects (Kenawy 2001). Antibacterial testing can be conducted using various methods, including agar diffusion and dilution/microdilution methods. The diffusion method can utilize disk paper or well method to determine the capability of a sample to inhibit bacterial growth by comparing the results with existing antibiotics. On the other hand, the dilution/microdilution method is used to assess the potency of a sample as an antibacterial agent (Balouiri et al. 2016).

Methanol skin extract of various *A. cepa* variants, obtained through sonication-assisted extraction, has shown potential as an antimicrobial agent, particularly against Gram-negative bacteria such as *S. typimurium* and Gram-positive bacteria such as B. cereus (Sagar and Pareek 2020). These findings align with the results reported by Fredotović et al. (2021), who demonstrated the antimicrobial activity of waste extract from A. cepa L, with MIC values of 500 μg/mL against MRSA (multidrug-resistant *S. aureus*), *S. pyogenes*, and *B. cereus*. In a study by Yousufi (2012), the antibacterial activity of ethanol, chloroform, and aqueous extracts of *A. cepa* was evaluated using the Kirby-Bauer method, which showed inhibition zone diameters of more than 11 mm against *E. coli* and *K. pneumoniae*.

Ethanol extract of *A. cepa* at a concentration of 150 mg/mL exhibited antibacterial activity, inhibiting *E. coli*, *S. aureus*, and *P. aeruginosa* with inhibition zone diameters of 10 mm, 14 mm, and 9 mm, respectively (Oyawoye et al. 2022). Another study demonstrated that the extract of fresh *A. cepa* resulted in inhibition zone diameters of 20 mm, 17 mm, and 15 mm against *S. pyogenes*, *S. aureus*, and *E. coli*, respectively (Shinkafi et al. 2013).

In a study by Heidary et al. (2022), *A. cepa* exhibited potential as a phytomedicine capable of inhibiting *C. albicans* and suppressing major fungal virulence factors. Sittisart et al. (2017) demonstrated that an *A. cepa* extract from Thailand, at a concentration of 80%, had antifungal activity against the mycelial growth of the pathogenic fungus, *Phomopsis* spp.

Furthermore, other research reported that *A. cepa* extract exhibited inhibitory effects against multidrug-resistant bacteria, including multi-drug resistant *S. aureus* (MRSA) (Fredotović et al. 2021). Kyung (2012) conducted a study showing that *A. cepa* extract possessed antibacterial activity against multi-drug resistant M. tuberculosis. In addition, Ahmadi et al. (2018) reported that *A. cepa* showed potential as an antiviral agent against avian influenza subtype H9N2, reducing mortality and possibly inhibiting the propagation of the virus in chicken egg embryos.

Anti-inflammatory

Sato et al. (2015) was reported that *A. cepa* have a potency as a antiallergic activity for type I hypersensitive, with IC_{50} value is a 20.8 μg/mL. From the correlation coeffecient between antiallergic activities and HPLC chromatogram constituent from *A. cepa* noted that quercetin 4'-glucoside has a highly-positive correlation with the antiallergic activities.

The effect of anti-inflammatory testing was done by carrageenan-induced with experimental animals. Oyewusi et al. (2021) were reported that 200 mg/kg methanol extract of *A. cepa* bulb, showed inhibition of inflammatory activity 62.50% on 30 min, which significantly higher than indomethacin (15.63%) at 10 mg/kg.

Ghorani et al. (2018) reported that the activity of the water-ethanol extract of A. cepa (with three concentrations of 0.175, 0.35, and 0.7 mg/mL) on tracheal response, pneumonia cells and levels phospholipase A2 (PLA2) levels in bronchoalveolar fluid (BALF) of rats with asthma have been tested. *A. cepa* at any concentration was able to reduce the total white blood cell count (WBC) and PLA2 levels compared with the asthmatic group. Decreased tracheal reactivity has been shown with extracts of *A. cepa* at concentrations of 0.35 and 0.7 mg/mL. Meanwhile, the effect of reducing the number of monocytes compared with the asthmatic group was demonstrated by the *A. cepa* extract with the highest concentration (0.7 mg/mL). So, from this report *A. cepa* was potential for asthma treatment.

Sato et al. (2015) reported that *A. cepa* exhibits potential as an antiallergic agent for type I hypersensitivity, with an IC_{50} value of 20.8 μg/mL. The correlation coefficient analysis between antiallergic activities and HPLC chromatogram constituents from *A. cepa* indicated a highly positive correlation between quercetin 4'-glucoside and the antiallergic activities.

The anti-inflammatory effect was evaluated using carrageenan-induced inflammation in experimental animals. Oyewusi et al. (2021) reported that the methanol extract of *A. cepa* bulb at a dose of 200 mg/kg showed a 62.50% inhibition of inflammatory activity after 30 minutes, which was significantly higher than that of indomethacin (15.63%) at a dose of 10 mg/kg.

Ghorani et al. (2018) conducted a study to evaluate the activity of a water-ethanol extract of *A. cepa* (at concentrations of 0.175, 0.35, and 0.7 mg/mL) on tracheal response, pulmonary cells, and phospholipase A2 (PLA2) levels in bronchoalveolar fluid (BALF) of rats with asthma. The *A. cepa* extract at all concentrations was able to reduce the total white blood cell count (WBC) and PLA2 levels compared to the asthmatic group. Decreased tracheal reactivity was observed with *A. cepa* extracts at concentrations of 0.35 and 0.7 mg/mL. Moreover, the highest concentration of *A. cepa* extract (0.7 mg/mL) demonstrated a significant reduction in the number of monocytes compared to the asthmatic group. Therefore, based on this report, *A. cepa* shows potential for the treatment of asthma.

Antiplatelet

The antiplatelet activity was assessed using a turbidimetric assay, and the extent of aggregation was measured using the Lumi-aggregatometer. The methanol extract of *A. cepa* bulb demonstrated potency as an antiplatelet agent. Ko et al. (2018) reported that the activity of antiplatelet agents is affected by flavonols such as quercetin and quercetin glucosides. Quercetin showed a significant effect against platelet aggregation compared to its glucosides. However, the combination of quercetin and its glucosides was found to be more effective than quercetin alone. The exact mechanism of this synergistic effect is still unknown (Ko et al. 2018).

Conclusion

Research investigating the potency of *A. cepa* is still ongoing, with new studies published each year in reputable journals. *A. cepa* has long been recognized as a traditional medicine used for the treatment of various conditions, including diabetes, various types of cancer, cough, influenza, dermatological problems, diarrhea, menstrual and abdominal pain, and malaria. Phytochemicals such as polyphenols, flavonoids, steroid saponins, furostanol saponins, and sulfur compounds have been reported in *A. cepa* and are believed to be responsible for its bioactivities. These bioactivities include antioxidant activity, which is associated with other beneficial effects such as anti-aging, antidiabetic, and anticancer properties. Additionally, *A. cepa* exhibits antimicrobial and antiplatelet activities.

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