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Review Article

# A review of botanical, phytochemical, and pharmacological properties of *Alcea rosea* L.

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#### Abstract

**Background and aims:** This article was written to better introduce *Alcea rosea* as a valuable medicinal plant to the medical and pharmaceutical communities and the general public for industrial and traditional uses as a valuable medicinal plant.

**Methods:** The results were gathered from scientific papers and databases to find flavonoids, phenolic acids, amino acids, fatty acids, anthocyanins, polysaccharides, and pharmacological activities in *A. rosea*. Sixty-two articles were found, and 51 were used for our final results.

**Results:** Studies have shown that flowers, roots, seeds, and other parts of the plant exert antioxidant, antimicrobial, anti-inflammatory, cytotoxic, sedative, analgesic and anti-cough effects due to the presence of valuable phytochemical compounds such as anthocyanins, pectin, starch, monosaccharide, disaccharide, mucilage, flavonoids (hypolaetin-8-glucoside, isoquercitrin, kaempferol, caffeic acid, p-coumaric acid), coumarins, scopolamine, phytosterol, tannins, asparagine, and certain amino acids.

**Conclusion:** *Alcea rosea*, as a rich source of secondary metabolites, can have diverse applications in medical and food research.

Keywords: Alcea rosea, Botany, Morphology, Pharmacological properties, Phytochemistry

### Introduction

Most of the information available on medicinal plants has been practically obtained from experiences with traditional uses (1). Medicinal plants contain substances with medicinal properties that may be used directly or as raw materials for the synthesis of commercially valuable drugs (2). Researchers have recently sought to replace chemical drugs with nature-based medications to prevent many drug-related problems. However, medicinal plants also have chemicals that, as with synthetic drugs, have the potential to cause relatively severe adverse side effects (2), so identifying the bioactive ingredients of medicinal plants and investigating their effects and the unpredictable effects of these compounds can help determine the use of these plants (1,3). Humans have used A. rosea for pharmaceutical purposes since 6000 years ago (4). In recent years, studies have shown that flowers, roots, seeds, and other parts of the plant exert antioxidant, antimicrobial, anti-inflammatory, cytotoxic, sedative, analgesic, anti-cough, immunomodulatory, and antibiotic effects (5) due to the presence of valuable phytochemical compounds such as anthocyanins, pectin, starch, monosaccharide, disaccharide, mucilage, flavonoids (hypolaetin-8-glucoside, isoquercitrin, kaempferol, caffeic acid, p-coumaric acid), coumarins,

erties, Phytochemistry scopolamine, phytosterol, tannins, asparagine, and certain amino acids (6-8). Therefore, Alcea rosea, as a rich source of secondary metabolites, can have diverse applications in medical and food research. This study aimed to investigate morphological characteristics, physicochemical properties, phytochemical compounds (phenol, flavonoids, fatty acids, proteins, and polysaccharides), and therapeutic properties of *A. rosea* to identify its properties

#### **Materials and Methods**

and help conduct subsequent studies.

Information from herbal books, authoritative journals, and articles retrieved from databases such as Google Scholar, PubMed, Science Direct, and Scopus search engine using keywords, medicinal activities, physicochemical properties, traditional medicine, modern medicine, phytochemical compounds, and commercial products were collected in *Alcea rosea*. And then, after reviewing the primary articles, more detailed searches were done again, for example, in phytochemical compounds, the words flavonoids, phenolic acid, amino acid, fatty acid, anthocyanins, polysaccharides, and in modern medicine, the words Anticancer Activity, Antidiabetic Activity, Kidney Stone, Antioxidant Activity, Antimicrobial Effect, Immune System, Antiestrogenic Effects were searched

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Received: October 9, 2022 Accepted: November 19, 2023 ePublished: December 28, 2023 to get complete information. The text of the abstracts of the articles and the titles of the chapters of the books were checked in terms of thematic connection with the items mentioned above, and then the unrelated items were removed from among them. In the initial search, 62 cases were found, and after reviewing the findings in the final analysis, 51 of them were used. Then the report studied and used the details of articles, chapters, and different parts of flora and books.

### Results

Classification, geographical distribution, botanical characteristics, and reproduction methods Classification and local names of *A. rosea* in some countries are presented in Table 1. This plant spreads worldwide, including the western Mediterranean region, to the center of Asia. This species is cultivated as an ornamental and medicinal plant or grows wild as a weed on the city's outskirts and the side of roads (9,10). Sunny regions are suitable for plant growth (11). The form of the plant is erect with few branches (12,13), it is 0.5 to 2 meters high, and its stem diameter is 2.4 to 3 cm. The leaves are large (7.5 to 12.5 cm in diameter) with 5-7 deep lobes. The flowers (Figure 1) are more significant than 10 cm in diameter, have different colors, and are in the Racom's inflorescence (12). The seed is kidney-shaped and disc-like, its edges are trichomes, and its size is 6 mm. The color of the seeds is brown to black and white, which



Figure 1. A: A. rosea. (16), B: Pollen grain of A. rosea (15), C: Peltate glands (type-II) on the abaxial surface of A. rosea

 Table 1. Classification and local names of A. rosea in some countries

| Vernacular names (6)               | Plant taxonomy (14)   |           |                     |
|------------------------------------|---|-----------|---------------------|
| Malta: Hollyhock,Malvarose         | Arabic: Khatma wardi  | Kingdom:  | Plantae plants      |
| Roumanian: Nalba de gardina        | Chinese: Shu k'ui   | Division: | Magnoliopsida       |
| Russian: Chernaya roja, Shtok rosa | English: Hock Herb, Hollyhock, Round Dock                             | Class:    | Magnoliopsida       |
| Spanish: Malva arborea, Malva loca | French: Alcee, Alcee rose, Althee rose, Mauve rose, Pass rose         | Ordea:    | Malvaceae           |
| Kannad: Doddabindigaegidda         | German: Augenpappel, Baummalve, Baumrose,<br>Gartenmalve, Rosenpappel | Genus:    | Alcea rosea Linn    |
| Italian: Malvarose, Malvoni        | Greek: Altaia   | Synonyms: | Althaea rosea Linn* |

\*Althaea rosea (L.) Cav. is a synonym of Alcea rosea L. The record derives from WCSP (in review) (data supplied on 2012-03-23), which reports it as a synonym with original publication details: Diss. 2: 91 1786 (IPNI: http://ipni.org/urn:lsid:ipni.org:names:558713-1.).

becomes distinct when the seed ripens. The pollen grains are spherical with a diameter of about 115 (132) 142  $\mu$ m. At the pollen grain's surface, some stomata are at a pore size of 2 (4) 5  $\mu$ m (14). In their study in 2010, Shaheen et al. observed that the maximum size of *A. rosea* pollen grain is 125 (143.2 ± 4.2) 162.5  $\mu$ m, and most stomata are diacytic, stellate trichomes and monomorphic (15).

Reproduction of this plant is often done through seed, but the division of the root is also used ("The Wealth of India," 1985); another way of reproducing this plant is tissue culture. Among the explants, cotyledons are more appropriate for callosing and organogenesis of *A. rosea* (17-19).

## Physicochemical characteristics

The results of a study on A. rosea seeds showed that

moisture content was  $(8.2 \pm 0.38\%)$  and inflation index  $(5.3 \pm 0.16)$  ml. Total ash, acid-insoluble, and watersoluble ash were  $7.3 \pm 0.32$ ,  $1.48 \pm 0.16$ , and  $3.33 \pm 0.24$ , respectively (20).

## Phytochemical evaluation

Phytochemical compounds are secondary plant metabolites that may not be necessary for the plant but have essential properties, such as antioxidant (21), antimicrobial, antifungal (22,23), anti-inflammatory, and antidiabetic properties that are also used to prevent and treat diseases (9,24). These compounds of *A. rosea* are rich in alkaloids, carbohydrates, fatty acids, phenolic compounds, glycosides, flavonoids (25), metals, amino acids, and monosaccharides (26). The secondary metabolites reported to exist in *A. rosea* are shown in Table

| Mino acidIdentification, Medicania, Soluciene, Lysine, Phenylalanine, Histidine, Anginene(27)AngeInferencia Cadi(28)Fatty acidGaranetic Cadi(29)AngeCarpenyl-Cod, Sigmasterol, p-Stotated(23)AngeCadio Cadio Cadi   | Group           | Compound  | Reference             |  |
|---|-----------------|---|-----------------------|--|
| Ideicad         Ideicad         Ideicad           Barback         Ideicad         Ideicad           Ideicad         Ideicad <td< td=""><td>Amino acid</td><td>Valine, Threonine, Methionine, Isoleucine, Leucine, Lysine, Phenylalanine, Histidine, Arginine</td><td>(27)</td></td<>  | Amino acid      | Valine, Threonine, Methionine, Isoleucine, Leucine, Lysine, Phenylalanine, Histidine, Arginine  | (27)                  |  |
| Fatty acid         Plantic acid, Stearie acid, Oleic acid, Linoleic acid, Minstin         (6,29.2)           a-Tempol/CAC, Stigmatend, P-Tokaldehyde, P-Stosterol         (6,20,00)         (3,34)           Phenolic acid         Seringi, p-thydroxybenzoic, p-Comaric, Ferolic acid, Caffeic, Vanillic, p-thydroxyphenylacetic acid         (3,34)           Phenolic acid         Galora         (3,34)           Mithy Cappendic acids         Galora         (3,14)           Seringi, p-thydroxybenzoic acids         Galora         (3,14)           Mithy Cappendic acids         Galora         (3,14)           Mithy Cappendic acids         Galora         (3,14)           Mithy Cappendic acids         Galora         (3,12)           Mithy Cappendic acids         Galora         (5,12,35,38)           Quecetin-3-Oph-D-glucorynanoide, Cappendic acids, Cappendicacids, Cappendicids, Cappendic acids, Cappendic acids, Cappendic a   |                 | Linoleic acid   | (28)                  |  |
| <form>         elaquenda       faquenda       (6,29,3)         handwice       faquenda       (1,3,1)         handwice       (1,3,1)       (1,3,</form>  | Fatty acid      | Palmitic acid, Stearic acid, Oleic acid, Linolenic acid, Linoleic acid, Mirstin   | (6,29-32)             |  |
| Beach         Big         Big </td <td></td> <td>α-Terpenyl-OAc, Stigmasterol, p-Tolualdehyde, β-Sitosterol</td> <td>(6,29,30)</td>   |                 | α-Terpenyl-OAc, Stigmasterol, p-Tolualdehyde, β-Sitosterol  | (6,29,30)             |  |
| Phenolic acid         Glarogenic         Glarogenic           Information         Allexplic acid         Add           Information         Add         Add           Information  |                 | Seringic, <i>p</i> -Hydroxybenzoic, <i>p</i> -Comaric, Ferrolic acid, Caffeic, Vanillic, <i>p</i> -Hydroxy-phenylacetic acid, <i>m</i> -Hydroxybenzoic acids  | (33,34)               |  |
| Aliquicacid(A)Remperol-3-Op-Deglucopyranoside(3)Remperol(3,2,3,3,3,3,3,3)Quercetin(3,2,3,3,3,3,3,3)Quercetin-3-Op-Dp-gluconopyranoside-3-Op-D-glucopyranoside, 3-Op-D-glucopyranoside, 3-Op-D-gl  | Phenolic acid   | Chlorogenic   | (33)                  |  |
| kampadia         (3)           kampadia         (3) <td></td> <td>Salicylic acid</td> <td>(34)</td>  |                 | Salicylic acid  | (34)                  |  |
| kampendi         (51,23,53)           kuencin         (51,23,53,33,73)           kuencin         (51,23,53,73,73)           kuencin         (51,23,73,73)           kuencin         (51,23,73,73) <td></td> <td>Kaempferol-3-<i>О</i>-β-D-glucopyranoside</td> <td>(35)</td>   |                 | Kaempferol-3- <i>О</i> -β-D-glucopyranoside   | (35)                  |  |
|   |                 | Kaempferol  | (6,12,35-38)          |  |
| Iudoin         (3)           Buiconic Acade Deglacorono pranoside S-CP-D sulconyranoside S-OP-D-rutinoside Kaempferol S-OP-D-glucoside.         (3)           Buiconic Kaempferol S-OP-Deglacorono pranoside S-OP-D-rutinoside Kaempferol S-OP-Deglacorono pranoside S-OP-D-rutinoside Kaempferol S-OP-Deglacorono pranoside S-OP-D-papelocopyranoside S-OP-D-papelocopyranoside S-OP-DP-papelocopyranoside S-OP-DP-PapeloC-DP-PapeloC-DP-PapeloC-DP-PapeloC-DP-PapeloC-DP-Papelo-Papelo-Papelocopyranoside S-OP-DP-PapeloC-DP-PapeloC-DP-   |                 | Quercetin   | (6,12,28,29,33,37,38) |  |
| Biologic Resemption 3 - 0-β - 0-glucoside. B-C-β - 0-glucosytanoside, 3-0-β - 0-tutinoside, Kaemption 4-0-β - 0-glucoside.<br>Biologicoside, Kaemption 3 - 0-β - 0-glucoside.<br>Disputor Asemption 3 - 0-glucoside.<br>Disputor Asempti |                 | Luteolin  | (33)                  |  |
| Flavonoida     Biblydrokaempferol-4-O-glucopyranoside_Diblydrokaempferol-3-O-β-D-glucopyranoside_Apigenin,<br>Kampferol-3-O-l6*-(f-courany)I)-β-D-glucopyranoside_Kaempferol-3-O-β-D-glucopyranoside_Apigenin,<br>Kampferol-3-O-glucoside     (39)       Isopercetin     (22,22,32)       Kampferol-3-O-glucoside     (31,23,33)       Isopercetin     (31,23,33)       Couraction     (31,23,33)       Isopercetin     (31,23,33)       Couraction     (31,23,33)       Isopercetin     (31,33)       Isopercetin     (32,33)       Isopercetin     (32,33)       Isopercetin     (31,33)       Isopercetin     (32,33)       Isopercetin     (32,33)       Isopercetin     (32,33)       Isopercetin     (32,33)  | Flavonoids      | Quercetin-3- $O$ - $\beta$ -D-glucuronopyranoside-8-C- $\beta$ -D- glucopyranoside, 3- $O$ - $\beta$ -D-rutinoside, Kaempferol -4'- $O$ - $\beta$ -D-glucoside, Kaempferol -3 - $O$ - $\beta$ -D-glucoside.   | (35)                  |  |
| Isolate continue       Instance         Instance       Instance         <   |                 | Dihydrokaempferol-4- <i>O</i> -glucopyranoside, Dihydrokaempferol-4'- <i>O</i> - $\beta$ -D-glucopyranoside, dihydrokaempferol, Kaempferol-3- <i>O</i> -[6"-(E-coumaroyl)]- $\beta$ -D-glucopyranoside, Kaempferol-3- <i>O</i> - $\beta$ -D-glucopyranoside, Apigenin, Kaempferol-3- <i>O</i> - $\alpha$ -L-rhamnopyranosyl-(1"" $\rightarrow$ 6")- $\beta$ -dglucopyranoside | (39)                  |  |
| Kaempferol-3-O-glucoside       (12,28,29)         Tigonelline       (40)         Glycine betaine       (6,12,37,38)         Coumarin       (6,12,37,38)         Delphinidin-3-O-glucoside, Delphinidin-3-O-rutinoside, Cyanidin-3-O-glucoside, Malvidin-3-O-glucoside, Mal  |                 | lsoquercetin  | (12.20.20)            |  |
| Inigonelline       Addeduce         Inigonelline       Addeduce         Inigonelline       (A12,A73,A13)         Inigonelline       (A12,A73,A13)         Inigonelline       (A12,A23,A13)         Inigonelline       (A12,A23,A13)         Inigonelline       (A12,A23,A13)         Inigonelline       (A12,A23,A13)         Inigonelline       (A12,A23,A13)         Inigonelline       (A12,A23,A13)         Inigonelline       (A13,A13)         Inigonelline, Petrinidin-3-O-glucoside, Malvidin-3-O-glucoside, M  |                 | Kaempferol-3-O-glucoside  | (12,20,29)            |  |
| Glycine betaine         (40)           Coumarin         (6,12,37,38)           Quadrin         (6,12,37,38)           Polphinidin-3-O-glucoside, Delphinidin-3-O-rutinoside, Cyanidin-3-O-glucoside, Malvidin-3-O-<br>malonylglucoside, Malvidin-3-O-thannosylglucoside, Malvidin-3-O-glucoside, Malvidin-3-O-<br>malonylglucoside, Malvidin-3-O-thannosylglucoside, Myricetin-3-O-glucoside, Malvidin-3-O-<br>malonylglucoside, Luteolin-4'-O-glucoside, Myricetin-3-O-glucoside, Cyanidin-3-O-<br>malonylglucoside, Luteolin-4'-O-glucoside, Myricetin-3-O-glucoside, Dolphinidine,<br>Polphinidine, Petotinidine, Malvidine, Dolphinidine, Phetodine and Malvydine from (3-O-glucoside), Dolphinidine,<br>Penthidine and Malvydine from (3,5-di-O-glycosides)         (42)           Dolphinidine, Petotinidine, Malvidine, Dolphinidine, Phetodine and Malvydine from (3-O-glucoside), Dolphinidine,<br>Penthidine and Malvydine from (3,5-di-O-glycosides)         (43)           Quadrametric         (43)         (44,7)           Rannose, Xylitol         (44,47)         (44,47)           Polysaccharie         (26,44,47)         (44,47)           Polysaccharie         (20)         (44,47)           Karnose, Xylitol         (44,47)         (44,47)           Quadrametric         (45)         (45)           Glacturonol, Limonene, Phellandrene, β-Stitosterol, besides sucrose, p-Tolualdehyde, a-terpenyl acetate         (45,48)           Glacturonorhamnans, Arabinans, Glucans, Arabinogalactans, Glucans         (46,12,37,38)           Hemicellulose, Uranic aci  |                 | Trigonelline  | (40)                  |  |
| Counaria(6,12,37,38)AnthocyaniaCayaidine(12,28,29)Delphinidin-3-O-glucoside, Delphinidin-3-O-rhamnosylglucoside, Malvidin-3-O-glucoside, Malvid   |                 | Glycine betaine   |                       |  |
| RathocyaniaCyanidine(12,82,9)AnthocyaniaDelphinidin-3-O-glucoside, Delphinidin-3-O-rutinoside, Cyanidin-3-O-glucoside, Malvidin-3-O-glucoside, Malvidin-3-O-gluc  |                 | Coumarin  | (6,12,37,38)          |  |
| AnthocyaniaDelphinidin-3-O-glucoside, Delphinidin-3-O-rutinoside, Cyanidin-3-O-glucoside, Malvidin-3-O-<br>Petunidin 3-O-glucoside, Petunidin-3-O-rhamosylglucoside, Malvidin-3-O-glucoside, Malvidin-3-O-<br>malonylglucoside, Malvidin-3-O-rhamosylglucoside, Myricetin-3-O-glucoside, Kaempferol 3-O-rutinoside,<br>Kaempferol-3-O-glucoside, Luteolin-4'-O-glucoside(41)Dolphinidine, Petotinidine, Malvidine, Dolphinidine, Phetodine and Malvydine from (3-O-glucoside), Dolphinidine,<br>Petutidine and Malvydine from (3,5-di-O-glycosides)(42)Luteolin 8-C-glucoside, 7-methyl ethers(43)Galactronic Acid, Glucuronic Acid, Ramenose, Arabinose, Galactose(26,39,44-46)Manose, xylitol(26,44,47)Polysaccharide(26,44,47)Polysaccharide(28,48)Galactronorhamnans, Arabinans, Glucans, Arabinogalactans, Glucans(28,48)Hemicellulose, Uranic acid(26,12,37,38)Hemicellulose, Uranic acid(26)   |                 | Cyanidine   | (12,28,29)            |  |
| Dolphinidine, Petotinidine, Malvidine, Dolphinidine, Phetodine and Malvydine from (3-O-glucoside), Dolphinidine,<br>Pethidine and Malvydine from (3,5-di-O-glycosides)(42)Luteolin 8-C-glucoside, 7-methyl ethers(43)Galactronic Acid, Glucuronic Acid, Ramenose, Arabinose, Galactose(26,39,44-46)Glucose(26,44,47)Mannose, xylitol(44,47)Polysaccharide(45)Starch, Lignin(28,48)Galacturonorhammans, Glucans, Arabinogalactans, Glucans(6,12,37,38)Hemicellulose, Uranic acid(26)   | Anthocyanins    | Delphinidin-3-O-glucoside, Delphinidin-3-O-rutinoside, Cyanidin-3-O-glucoside, Cyanidin-3-O-rutinoside, Petunidin 3-O-glucoside, Petunidin-3-O-rhamnosylglucoside, Malvidin- 3-O-glucoside, Malvidin-3-O-malonylglucoside, Malvidin-3-O-rhamnosylglucoside, Myricetin-3-O-glucoside, Kaempferol 3-O-rutinoside, Kaempferol-3-O-glucoside, Luteolin-4'-O-glucoside             | (41)                  |  |
| Luteolin 8-C-glucoside, 7-methyl ethers(43)Galactronic Acid, Glucuronic Acid, Ramenose, Arabinose, Galactose(26,39,44-46)Glucose(26,44,47)Nannose, xylitol(44,47)Cyclohexanol, Limonene, Phellandrene, β-Sitosterol, besides sucrose, p-Tolualdehyde, α-terpenyl acetate(45)Starch, Lignin(28,48)Galacturonrhammans, Arabinans, Glucans, Arabinogalactans, Glucans(6,12,37,38)Hemicellulose, Uranic acid(26)  |                 | Dolphinidine, Petotinidine, Malvidine, Dolphinidine, Phetodine and Malvydine from (3-O-glucoside), Dolphinidine, Penthidine and Malvydine from (3,5-di-O-glycosides)  | (42)                  |  |
| Galactronic Acid, Glucuronic Acid, Ramenose, Arabinose, Galactose(26,39,44-46)Glucose(26,44,47)Mannose, xylitol(44,47)PolysaccharidesCyclohexanol, Limonene, Phellandrene, β-Sitosterol, besides sucrose, p-Tolualdehyde, α-terpenyl acetate(45)Starch, Lignin(28, 48)Galacturonorhamnans, Arabinans, Glucans, Arabinogalactans, Glucans(6, 12, 37, 38)Hemicellulose, Uranic acid(26)   |                 | Luteolin 8-C-glucoside, 7-methyl ethers   | (43)                  |  |
| Glucose(26,44,47)Mannose, xylitol(44,47)PolysaccharidesCyclohexanol, Limonene, Phellandrene, β-Sitosterol, besides sucrose, p-Tolualdehyde, α-terpenyl acetate(45)Starch, Lignin(28, 48)Galacturonorhamnans, Arabinans, Glucans, Arabinogalactans, Glucans(6, 12, 37, 38)Hemicellulose, Uranic acid(26)   |                 | Galactronic Acid, Glucuronic Acid, Ramenose, Arabinose, Galactose   | (26,39,44-46)         |  |
| Mannose, xylitol(44,47)PolysaccharidesCyclohexanol, Limonene, Phellandrene, β-Sitosterol, besides sucrose, p-Tolualdehyde, α-terpenyl acetate(45)Starch, Lignin(28, 48)Galacturonorhamnans, Arabinans, Glucans, Arabinogalactans, Glucans(6, 12, 37, 38)Hemicellulose, Uranic acid(26)  |                 | Glucose   | (26,44,47)            |  |
| PolysaccharidesCyclohexanol, Limonene, Phellandrene, β-Sitosterol, besides sucrose, p-Tolualdehyde, α-terpenyl acetate(45)Starch, Lignin(28, 48)Galacturonorhamnans, Arabinans, Glucans, Arabinogalactans, Glucans(6, 12, 37, 38)Hemicellulose, Uranic acid(26)   | Polysaccharides | Mannose, xylitol  | (44,47)               |  |
| Starch, Lignin(28, 48)Galacturonorhamnans, Arabinans, Glucans, Arabinogalactans, Glucans(6, 12, 37, 38)Hemicellulose, Uranic acid(26)   |                 | Cyclohexanol, Limonene, Phellandrene, $\beta$ -Sitosterol, besides sucrose, p-Tolualdehyde, $\alpha$ -terpenyl acetate  | (45)                  |  |
| Galacturonorhamnans, Arabinans, Glucans, Arabinogalactans, Glucans(6, 12, 37, 38)Hemicellulose, Uranic acid(26)   |                 | Starch, Lignin  | (28, 48)              |  |
| Hemicellulose, Uranic acid (26)   |                 | Galacturonorhamnans, Arabinans, Glucans, Arabinogalactans, Glucans  | (6, 12, 37, 38)       |  |
|   |                 | Hemicellulose, Uranic acid  | (26)                  |  |

2, and the schematic structure of some of its compounds is in Table 3.

## *Pharmacological activities Therapeutic uses in traditional medicine*

In different countries of the world (Ecuador, Saudi Arabia, India, Italy, etc), decoction, infusion, crude, ointment of the flower, root, stem, and seeds of *A. rosea* are traditionally used in the treatment of cough, asthma, throat infection, dysuria, rash, kidney stones and pain,

Table 3. The schematic structure of some of the compounds that have been reported to exist in A. rosea

| Molecular Structure                                 | Isolated Compound                         | Reference |
|---|---|-----------|
|   | Dihydrokaempferol-4'-O glucopyranoside    | (39)      |
| HO<br>HO<br>CI<br>O<br>D-β-glucosyl<br>D-β-glucosyl | Malvidin-3,5-diglucoside                  | (49)      |
| HO<br>HO<br>OH<br>OH<br>O<br>D-β-glucosyl           | Astragalin                                | (49)      |
|   | Rosea B                                   | (49)      |
| β-D-glucosyl -O +OH<br>OCH <sub>3</sub>             | Rosea A                                   | (49)      |
| HO<br>OGlu<br>OH<br>OH                              | Dihydrokaempferol-4'-O-β-dglucopyranoside | (39)      |
| HO<br>HO<br>OGlu                                    | Dihydrokaempferol                         | (39)      |

#### Table 3. Continued.



## Table 3. Continued.



Table 3. Continued.



and jaundice (50,51). This plant is a diuretic, refrigerant, sedative, softener, antipyretic, and astringent and is used for wound healing, bronchitis, reducing appetite, and angina, analgesic, arthritis, dysuria (6,12,52-56) . It is also used to improve blood circulation, constipation, reduce menstrual pain and bleeding (57), goiter, dermatitis, and liver diseases, mastitis, insect bites (50,51,57-59). In Iran, decoction, infusion, crude, ointment, and parts of *A. rosea* are traditionally used to treat digestive, respiratory, skin, cold, and migraine problems (60,61).

## *Therapeutic uses in modern medicine* <u>*Anticancer activity*</u>

The methanolic extract of the seed, root, and whole plant, in vivo conditions, has been reported to exert significant anticancer properties that control neoplastic cell changes in some of the cancer cell lines, such as JB6 + of the epidermis, in condition vivo (5,55,62,63). The ethyl acetate extract of *A. rosea* seed has been reported to inhibit proliferation and colony formation dose-timedependently and to promote apoptosis, as confirmed by PARP cleavage and an increase in Bax expression, along with a reduction in BCL-xL protein levels in HCT116 and SW480 cells, respectively. In addition, *A. rosea* seed extract causes cell cycle arrest at the G0/G1 phase and

decreases cyclin D1. The ethyl acetate extract of A. rosea seed treatment also reduced the number and size of colon spheres in the cells dose-dependently and simultaneously decreased the ALDH1A1 and Dclk1 cancer stem cell markers. After treatment with A. rosea extract, relative levels of -catenin, Notch-ICD, Hes1, and EZH2 decreased. TOP-flash reporter activity used to measure Wnt signaling declined significantly after treatment, while overexpression of wild-type but not mutant EZH2 neutralized the inhibitory effects. In addition, WIF1 (a Wnt antagonist) promoter activity increased notably after A. rosea extract treatment, phenocopying an increase in WIF1 reporter activity after EZH2 knockdown. A. rosea extract inhibited tumor growth in vivo, most likely by lowering levels of EZH2, -catenin, cyclin D1, and Ki-67, as well as cancer stem cell markers (62). Methanolic extract of A. rosea root in vivo has been observed to significantly suppress neoplastic cell transformation by inhibiting EGF receptor (EGFR) kinase activity. After treatment with methanolic A. rosea extract root, EGFR activation by EGF was inhibited in EGFR + / + cells but not in EGFR-/- cells. In addition, MARC inhibited EGFinduced cell proliferation in EGFR-expressing murine embryonic fibroblasts (EGFR + / + ) (5).

## Antidiabetic activity

The *A. rosea* seed has shown antihyperglycaemic and antioxidant activities in rats with alloxan-induced diabetes. Methanolic and aqueous extracts at 300  $\mu$ g/kg reduce blood glucose levels and increase antioxidant levels in the liver tissue (59). Some other researchers have also reported the plant as an antidiabetic agent (64, 65).

## Kidney stone treatment

The hydroalcoholic extract of this plant significantly reduces the calcium oxalate deposits of the kidney and also decreases the urinary oxalate levels in the rats induced by ethylene glycol; in other words, it can be widely used to treat kidney stones due to its anti-urolithiasis and diuretic properties (55).

## Cardiovascular effects

Alcoholic extract of *A. rosea* L. flower increased the outflow of the coronary artery of the heart isolated from guinea pigs. It pronouncedly dilated the blood vessels in the rat's hind limbs. The extract produced a temporary hypotensive effect on anesthetic cats. It inhibited ADP-induced platelet aggregation and exerted an inhibitory effect on experimental thrombosis formation (66).

## <u>Hepatoprotective effects against acetaminophen-induced</u> <u>hepatotoxicity</u>

A histopathologic study of liver tissues showed that *A. rosea* extracts produced protective effects against acetaminophen-induced hepatic toxicity (67).

#### Antiestrogenic effects

Berger et al (68) and Dudek et al (33) reported that cinnamic acid derivatives, para-coumaric acid, ferulic acid, and p-hydroxybenzoic acid were found throughout *A. rosea* and had estrogenic activity. Researchers have also reported weak estrogenic activity in rat testis for the aqueous A. rosea extract (69). The latter study studied a methanolic extract containing more flavonoids than the aqueous one. The morphological and histo-enzymatic changes in the Leydig cells indicated that the methanolic *A. rosea* extract produced a direct but partial effect on rat testis. The insignificant changes in estradiol content and testicular testosterone suggest that the extract does not impair steroidogenesis (70).

#### *Effect on the immune system*

One study has confirmed the immunogenetic activity (64). Another study showed that aqueous extract of *A. rosea* produces the following effects on the immune system: Inducing a transient non-specific polyclonal response evidenced by the production of IL-4 in non-immunized, treated mice; initially boosting the output of anti-EA antibodies and IL-4, a T-helper two cytokines; and suppressing the production of gamma-interferon, a T-helper 1 cytokine (71).

## Antioxidant activity

Free radicals cause inflammation, cancer, cardiovascular disease, and osteoporosis; therefore, antioxidant compounds benefit human health and reduce oxidative stress. The antioxidant activity of A. rosea has already been reported (5, 35, 62, 72, 73). The antioxidant activity of methanolic extracts of aerial parts and flowers of A. rosea has been measured more frequently than that of the vegetative part (herbage). In the investigations of Liu et al (73), the antioxidant activity of aqueous, ethanol, butanol, and chloroform extracts A. rosea seed was measured using four superoxide anion scavenging, hydroxyl radical scavenging assay, superoxide dismutase activity assay, and DPPH assay. The aqueous extract had the most significant antioxidant activity in the DPPH method, superoxide dismutase activity assay, and superoxide anion scavenging assay. Butanol extract had comparatively more significant antioxidant activity in the hydroxyl radical scavenging assay. Antioxidant activity was directly related to the total phenolic content, so the h distilled water extracts found the highest total phenolic content. The chloroform extract exhibited the weakest antioxidant activity (73). Tyrosinase activity was reported to be inhibited by hydroalcoholic A. rosea extract (74). Differences in antioxidant activity are due to differences in the amounts of secondary metabolites, such as flavonoids, or the presence of other secondary antioxidant compounds that directly or indirectly produce this activity (75).

#### Antimicrobial Effect

Several studies have confirmed the antimicrobial effects (Tables 4 and 5) of this plant's different extracts (64, 76).

#### Other properties

The ethyl acetate extract showed cytotoxic activity against Brine shrimp (LC50 < 1000) (77), but this extract was even more active than umbelliferon (78) and colchicine (79). Choi et al (5) studied whether methanol extracts of A. rosea were cytotoxic in the mouse epidermal JB6 P + cells. Their results showed that methanol A. rosea extract at different doses did not affect the viability of JB6 P + cells (5). In addition, the compound kaempferol-3-O-[6"-(Ecoumaroyl)]-βd-glucopyranoside extracted from A. rosea has a potent cytotoxic activity on HepG-2 cell line with an IC50 of 3.822 µg/mL (6.434 µM) when compared to reference standard 5-Fluorouracil ( $IC_{50} = 0.9 \,\mu g/mL, 6.919$ µM) (63). Methanol and aqueous extracts of A. rosea seed showed nontoxic effects on the behavioral parameters in normal healthy rats. A survival rate of 100% was observed in animals treated with 50-300 mg/kg body weight (BW) of A. rosea extracts, while in the animals treated with the extracts at 350-500 mg/kg BW, the survival rate was 50-90% (59). The dry extract of this plant stem and root has been found to contain monosaccharides, oligosaccharides, mucus, microelements, and proteins. Therefore, the dry extract of this plant has therapeutic effects on asthma, bronchitis, respiratory tract infection, and inflammatory

### disease (26).

## **Commercial products**

*Alcea rosea* makes paper bags (80) and edible colors (71). So far, no pharmaceutical and cosmetic products have been reported to be produced from the Alcea genus.

#### **Discussion and Future Perspectives**

Results have shown that *A. rosea* is one of the most valuable medicinal plants with critical medicinal compounds such as mucilage and high phenolic compounds. This plant grows wild in Iran in abundance, which the general public traditionally collects to treat diseases. In addition, this plant is cultivated commercially and has been used to make many medicines. Hence, the economic significance of the medicinal *A. rosea* is undeniable. Due to the potential, and diverse applications of active ingredients of medicinal *A. rosea*, especially its medicinal compounds, their use can reduce the use of synthetic drugs that threaten the immunity of consumers. Hence, the importance of using the active ingredients of this plant multiplies the value of research related to this issue and prompts further

research on the other valuable and unknown properties of this plant to be used as a medicine for treating human diseases. The key that can be used in this research is the anti-inflammatory, analgesic, antifungal, and therapeutic effects for digestive, skin, respiratory, and other medicinal diseases of *A. rosea*, which is due to the presence of valuable medicinal compounds such as mucilage, which has been less investigated. It is also recommended to use this plant to develop cosmetic-medicinal products due to its potential.

### Conclusion

This research data will help you get to know this plant, its medicinal properties, and other uses in the medical, food, agricultural, etc. industries. Our research showed that *A. rosea* is one of the most important and widely used medicinal plants because it is used in the design of green spaces and gardens due to its beautiful appearance and also because of its valuable compounds; the traditional and modern uses of this plant and its therapeutic effects have been reported in various diseases. The information

Table 4. Antibacterial effects of different concentrations of Alcea rosea ethanol extract (80)

| Bacterial specie       |                            | Different concentrations of A. rosea ethanol extract |      |      |      |      |      |      |      |  |
|------------------------|----------------------------|--|------|------|------|------|------|------|------|--|
|                        |                            | Flower   |      |      |      | Leaf |      |      |      |  |
|                        |                            | 0.05   | 0.10 | 0.20 | 0.40 | 0.05 | 0.10 | 0.20 | 0.40 |  |
| Gram-positive bacteria | Bacillus anthracis         | 7  | 10   | 11   | 15   | 8    | 9    | 9    | 14   |  |
|                        | Bacillus cereus            | R  | R    | R    | 9    | R    | R    | 8    | 10   |  |
|                        | Staphylococcus aureus      | 10   | 13   | 17   | 18   | 8    | 8    | 10   | 13   |  |
|                        | Staphylococcus epidermidis | 9  | 10   | 15   | 19   | R    | 9    | 10   | 13   |  |
|                        | Listeria monocytogenes     | R  | R    | R    | 7    | R    | R    | 7    | 10   |  |
|                        | Streptococcus pyogenes     | 8  | 9    | 10   | 13   | 8    | 8    | 9    | 11   |  |
| Gram-negative bacteria | Escherichia coli           | R  | R    | R    | R    | R    | R    | R    | R    |  |
|                        | Salmonella Typhi           | R  | R    | 7    | 8    | R    | R    | R    | 8    |  |
|                        | Klebsiella pneumoniae      | 7  | 7    | 9    | 14   | 7    | 8    | 10   | 12   |  |
|                        | Pseudomonas aeruginosa     | R  | 8    | 9    | 13   | R    | R    | R    | R    |  |

R: Resistant, \*(6 mm) diameter disc.

Table 5. Antimicrobial activity of Alcea rosea extracts (81)

| Minu                                 | Inhibition zone (mm)* |    |    |   |   |    |    |   |  |
|--------------------------------------|-----------------------|----|----|---|---|----|----|---|--|
| Microorganisms                       | А                     | В  | С  | D | E | F  | G  | н |  |
| Escherichia coli ATCC 29998          | 9                     | 9  | 9  | 9 | 9 | 15 | -  | - |  |
| Escherichia coli ATCC 25922          | -                     | -  | -  | - |   | 14 | -  | - |  |
| Escherichia coli ATCC11230           | 10                    | 9  | 10 | 9 | 9 | 18 | -  | - |  |
| Staphylococcus aureus ATCC 6538P     | 8                     | 10 | 9  | 7 | 9 | 12 | -  | - |  |
| Staphylococcus aureus ATCC 29213     | -                     | 9  | 9  | 9 | 9 | 13 | -  | - |  |
| Staphylococcus epidermidis ATCC 1222 | 8                     | 10 | 10 | 9 | 8 | 12 | -  | - |  |
| Salmonella Typhimurium CCM 5445      | 8                     | 8  | 8  | 8 | 7 | 14 | -  | - |  |
| Enterobacter cloacae ATCC 13047      | -                     | -  | -  | - | - | 13 | -  | - |  |
| Enterococcus faecalis ATCC 29212     | -                     | -  | -  | - | - | 11 | -  | - |  |
| Pseudomonas aeruginosa ATCC 27853    | 9                     | 9  | 9  | 8 | 8 | 22 | -  | - |  |
| Candida albicans ATCC 10239          | -                     | -  | -  | - | - | -  | 18 | - |  |

A: Ethanol extract; B: n-Hexane extract; C: Ethyl acetate extract; D: Methanol extract; E: Water extract; F: Ceftazidime; G: Nystatin; H: Control (DMSO). \*Includes the diameter of the disc (6 mm). collected in this article can be a basis for further studies and help make herbal and natural medicines. In addition to knowing the importance of this medicinal plant, the necessity of cultivation and production of this medicinal plant and its secondary metabolites multiplies, which should be considered in the future.

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#### **Competing Interests**

Although one of the authors in this article is the journal's Editor-in-Chief, the whole process of reviewing and publishing this article is like other articles in the journal, and there is no difference in its review from other articles.

#### **Ethical Approval**

Not applicable.

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