ALCEA: TRADITIONAL MEDICINE, CURRENT RESEARCH AND FUTURE OPPORTUNITIES

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The genus *Alcea* consists more than 40 subspecies. Most of them were partly studied but some of them were not. In this review we will introduce the traditional medicinal knowledge and uses of this genus, summarize and discuss the modern research reports of the medicinal/biological activities of the various subspecies. Special attention will be paid to *A. rosea*, the most investigated subspecies of this genus. Clear emphasis will be laid upon some reported natural products isolated from subspecies of *Alcea*. Future possible studies will be suggested.

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Introduction

Subspecies of the genus *Alcea* are among the most spectacular flowering plants, they bloom with relatively large, very colorful flowers. According to the Barcode of Life Data (BOLD) Systems, the genus is native to Asia and Europe.[1,2] The number of subspecies that consist this genus is not definite, and it varies from 21 according to the "U.S. National Plant Germplasm System",[3] to 40 subspecies,[4] and even higher in some reports.

Most of the subspecies can be found in Asia, especially in Iran (34 ssp.) and Turkey (18 ssp.).[5,6] Humans have taken this genus with them, mainly *Alcea rosea*, while migrating to the "New World", and with the plants, the traditional medicine uses of them were aslo adopted.[7]

Traditional uses of *Alcea* subspecies

Peoples of Euroasia used the various subspecies of this plant genus since very ancient times. The extinct Neandarthal humans used *A. rosea* about 60000 years ago for medicinal and ritual purposes.[8]

In table 1, a summary of the traditional uses of *Alcea* subspecies is presented.

Biological and medicinal activities of *Alcea* subspecies (excluding *A. rosea*)

The reported biological/medicinal activities of the *Alcea* subspecies are of a wide variety, which includes most of the typical medicinal activities of plants, such as antioxidant, antimicrobial, antiviral, hepatoprotective and others. Along with that, it is interesting to notice some reports of last few years that present modern uses, such as nanomaterials synthesis (section 4). But it is also notable that these activities do not include psychoactive or mind-altering activities of the plants, their extracts or of natural products isolated from them. This might be understood on the basis of the low content of alkaloids (and closely active compounds) in the subspecies of *Alcea*, which have no reported toxic effects on humans and other mammals. In table 2, a summary of the biological/medicinal activities of *Alcea* subspecies is listed, as well as reported active natural products and chemical composition, if reported.

Biological and medicinal activities of *Alcea rosea*

Alcea rosea is the most investigated subspecies of *Alcea*. Most of the biological/medicinal activities that were mentioned in table 2 related to all other studied subspecies of *Alcea*, can also be found in publications related to *A. rosea*. The chemical composition was extensively studied, and despite the fact that it is not completely known yet, some of its constituents were widely tested for medicinal/biological activities. Moreover, in addition to its traditional medicinal uses, *A. rosea* was used for tarditional dye industry, and recent years in nanochemistry. Summary of research articles of *A. rosea* properties are shown in table 3.

Discussion and Future Opportunities

Antioxidant acticity was reported for some subspecies of *Alcea*: *acaulis*,[41] *apterocarpa*, *pallida*,[43] *hyrcana*,[49] *kurdica*,[51,52] *setosa*,[72] *rosea*.[92,93,95] All these studies indicate two important facts. One, the major compound family responsible for the antioxidant activity is polyphenols. Two, various extracts of differents parts of these plants vary in their antioxidant capacity, but all of them have strong capacities. When these polyphenols (aqueous extract of *A. rosea*) were force fed to rats, these animals, swam longer time than the control group.[94] This result suggests the need for more studies of the application of this activity in sports and food industry.

Table 1. Region-wise traditional use of Alcea sub-species

Subspecies	Country/Region	Part Used /Objective /Mode of Use
A. acaulis	Jordan	NS[b] .[9]
	Lebanon	Whole plant, flower/ cough, catarrh, respiratory infections, constipation/ infusion.[10]
A. angulata	Iran	Flower/ antitussive, febrifuge, treatment of pimples, laxative, depurative, treatment of gum swelling, mouth wounds, bone fracture/ NS.[11]
A. apterocarpa	Turkey	Root, shoots, herb/ vulnerary, anti-inflammatory, skin disorders, urinary system disorders, kidney stones, pulmonary disorders, intestinal disorders, stomach ailments, cough/ decoction, infusion.[12]
A. arbelensis	Iran	Flower/ constipation, coughs, sores/ infusion, decoction, crude.[13]
	Iran	Flowers/ constipation/ NS.[14]
A. aucheri	Iran	Flower/ antitussive, febrifuge, treatment of pimples, laxative, depurative, treatment of gum swelling, mouth wounds, bone fracture/ NS.[11]
	Iran	Leaf, flower/ colds, influenza, sore throat/ decoction.[15]
A. biennis	Turkey	Flowers/ bronchitis/ infusion, maceration.[16]
A. calvertii	Turkey	Root, herb/ vulnerary, anti- inflammatory, skin disorders, kidney stones, urinary system disorders, pulmonary disorders, stomach disorders/ decoction, infusion.[12] Flower/ respiratory system, coughs, infection, asthma/ maceration.[13]
	Iran	Flower/ asthma, coughs, infections, respiratory disorders/ extraction, infusion,
	Iran	maceration.[17]
A. damascena	Lebanon	Whole plant, flower/ cough, catarrh, respiratory infections, constipation/ infusion.[10] Flowers/ herbal tea/ infusion.[18]
	Syria	
A. dissecta	Turkey	Leaf/ injuries, asthma/ pounding, poultice.[12]
	Turkey	Leaves/ expectorant/ decoction.[19]
A. excubita	Turkey	Leaf, Flower/ vulnerary, expectorant, cold/ pounding , poultice.[12]
	Turkey	Leaves, flowers/ joint injuries/ decoction.[19]
A. fasciculiflora	Turkey	Root/ kidney stones, abscess, scabies/ decoction, poultice.[12]
A. flavovirens	Turkey	Root/ kidney stones, abscess, scabies/ decoction, poultice.[12]
	Iran	Flower/ stomachache.[13]
	Azarbaijan	Flower/ NS/ NS.[20]
A. koelzii	Iran	Flower/ infection, respiratory system/ decoction.[13]
A. kurdica	Iran	Flower/ Carminative in veterinary, coughs/ infusion.[13,17]
	Iraq	Flowers/ tonsillitis, gastric ulcers, duodenal ulcers, pneumonia, urinary tract infections, expectorant, alopecia/ infusion.[21]
A. lavateriflora	Iran	Flower/antitussive, febrifuge, treatment of pimples, laxative, depurative, treatment of gum swelling, mouth wounds, bone fracture/ NS.[11]
A. pallida	Turkey	Leaf/ demulcent, expectorant, diuretic, anthilitic, emollient/ herbal medicine commercial product.[22]
A. rechingeri	Iran	Flower/ , respiratory system/ decoction.[13]
A. rhyticarpa	Iran	Flower/ antitussive, febrifuge, treatment of pimples, laxative, depurative, treatment of gum swelling, mouth wounds, bone fracture/ NS.[11]
A. rosea	Iran	Flower/ antitussive, febrifuge, treatment of pimples, laxative, depurative, treatment of gum swelling, mouth wounds, bone fracture/ NS.[11]
	Ecuador	Whole plant/ kidney problems, used as tonic/ pounded .[23]
	Saudi Arabia	Leaves, branches, fruits/ carminative, deworming/ mixed with food of livestock.[24]
	India	Flowers, roots, whole plant/ cough, asthma, throat infection, urinary irritation. Kidney pain, aunndice, urinary irritation, bladder, dandruff, dermatitis, easy delivery, goitre, gynecological disorders, inflammation, emollient.[25]
	Italy	Leaf/ cough, cold, bronchitis/ boiled with wine, decoction .[26]
	India	Whole plant/ bleeding gums/ NS.[27]
A. rufescens	Jordan	NS/ NS/ NS.[28,29]
A. rugosa	Azerbaijan	NS/ respiratory system illnesses/ NS.[30]
A. setosa	Jordan	NS/ NS/ NS.[9,28,29]
	Turkey	Leaf/ expectorant, diuretic, emollient/ infusion.[12]
	Turkey	Leaf/ demulcent, expectorant, diuretic, anthilitic, emollient/ herbal medicine commercial product.[22]
	Palestine	Whole plant/ stomach and intestine pain, inflammation, asthma/ decoction.[31,32]
	Arab countries	Flower, leaf, root/ cough, cold, stomach pain, urinary system pain, female sex stimulant, anti-inflammatory, wound relief, skin laxative.[33]

		NS/ Inflammation/ NS.[34]
	Greco-Arab	Leaf/ hair care, cleaning the house against dust/ NS.[35]
	Turkey	Flower/ cough, / decoction.[36]
	Turkey	Flower/ cough, chest pain/ infusion .[37]
	Jordan	Leaves, roots/ wounds, vegetable, gastritis, marshmallows, ornamental, saline tolerant/
	Jordan	infution, dried powder.[38]
A. striata	Turkey	Leaf, flowers/anti-inflammatory, anemia, cough/ decoction, infusion.[12]
	Turkey	Leaf/ anemia/ decoction.[39]
A. tarica	Iran	Flower/ throat, joint pains, fever, respiratory system/ infusion, decoction, extraction.[13]
	Iran	Flower/ joint pains, coughs, fever, infections, respiratory system disorders/ decoction, infusion.[17]
NS	Iran	Flower/ wound, burn/ decoction, ointment.[40]

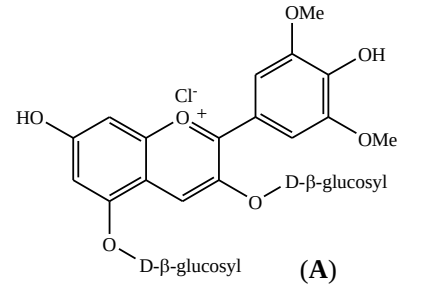
Table 2. Biological/medicinal activities of *Alcea* subspecies and active constituent

Alcea Subspecies	Biological-medicinal activities/ major active material(s)
A. acaulis	Antioxidant/ aqueous and methanolic extracts.[41]
A. angulata	Anti-hyperlipidemia/ alcoholic extract .[42]
A. apterocarpa	Antioxidant, anticholineesterase, antimicrobial/ acetone extract, detailed composition of essential oil is listed, fatty acid content is provided and phenolic content is detailed.[43]
A. aucheri	Heavy metal hyperaccumulator.[44]
A. digitata	NAR[c]/ phytochemical screening for biologically active compound families.[45]
	Relief of radiotherapy symptoms (mainly xerostomia)/ plant powder.[46]
A. flavovirens	NAR/ polysaccharide identified that contains: ribose, rhamnose, glucose, glucuronic acid, galacturonic acid (3:6:3:7:2).[47]
A. hyrcana	NAR/ polysaccharides isolated and analysed (%): uronic acids (32.3-45.7), glucose and galactose (24.5-38.7), arabinose (9.6-9.9), xylose (4.9-6.3), rhamnose (12.9-14.8).[48]
	Antioxidant (various methods)/ total phenolic content was determined.[49]
A. koelzii	NAR/ mineral content was determined (K, Ca, Mg, P, Fe, Mn, Cu, Zn).[50]
A. kurdica	Antioxidant/ total phenolic and total flavanoidic contents.[51]
	Antioxidant, antimicrobial, but not cytotoxic/ total phenolic content measured.[52]
	Acetylcholinesterase (ACE) inhibition/ methanolic extract.[53]
A. kusariensis	NAR/ Polysaccharides isolated from roots and stems, analysed with average values of uronic acids (39%), and the rest is composed of galactose, rhamnose with traces of glucose.[54]
A. longipedicellata	Anticariogenic against oral bacteria/ malvidin-3,5-diglucoside (from ethanolic extract).[55]
	Anticancer (gastric cancer cell line, AGS)/ malvidin-3,5-diglucoside with/without cisplatin.[56]
A. nudiflora	NAR/ Astraglin.[57]
	NAR/ Polysaccharides isolated and analysed with uronic acids (42%), and the rest is composed of glucose, galactose, arabinose, rhamnose with traces of xylose and mannose.[58]
	NAR/ polyprenols and triterpenoids were isolated and identified.[59]
	NAR/ Aliphatic contents was analyzed of two extracts of the aerial parts: EtOH, MTBE.[60]
	Immunomodulatory action/ polyprenols.[61]
A. pallida	Antioxidant, anticholineesterase, antimicrobial/ acetone extract, detailed composition of essential oil is listed, fatty acid content is provided and phenolic content is detailed.[43]
	Antistress/ infusion, no specific compound(s).[62]
	Resistance to allelophathy of some aromatic plants/ no specific compound was indicated to be resposible for this activity.[63]
	Accumulator of heavy metals, especially in leaves, where Pb had highest concentration/ Pb, Zn, Cu, Cd.[64]
	Liquid biofuels production by catalytic (zinc chloride on alumina) pyrolysis of stems/ bio-char, bio-oil, bio-gas.[65]
A. rhyticarpa	NAR/ investigation of semiemprical formula of dihydroxylignin content.[66]
	NAR/ investigation of the content and structures of dioxan lignins.[67]
	Antiviral activity/ no extract or sprcific compound is presented, but the article reviews research studies.[68]
A. rugosa	NAR/ four polysaccharides were isolated and analyzed. The average composition (%) is: rhamnose, 25.5; glucose, 17.1; galactose, 21.1; arabinose, 10.9; uronic acids, 25.4.[69]
	Diuretic and natriuretic/ kaempferol and its glycosides.[70]
	Sensitive to stagonolide, a phytotoxin isolated from *Stagonospora cirsii*.[71]
A. setosa	Antioxidant/ total phenolics and flavanoids were determined.[72]
A. sulphurea	Anti-inflammatory in mucociliary system of chicken trachea / aqueous and ethanolic extracts.[73]

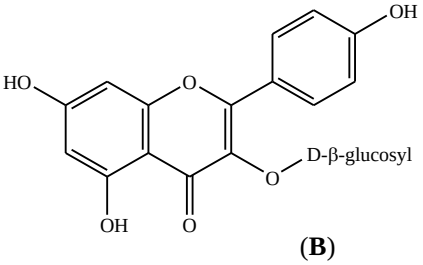
Table 3. Summary of research articles on *A. rosea*

Properties	Active Materials / Mode of Action
Fatty acids changes	Changes in the composition of fatty acids during plant life/ the general change is formation of
Coloring, pigmentation	Althaein, the blue pigment, 11% of all pigmentation.[75]
	Anthocyanins/ red dyes for food coloring.[76]
	Structure elucidation of the 12 compounds that give *A. rosea* (var. nigra) its color.[77]
Nanochemistry uses	Ethanolic extract as natural, low cost sensitizer for the synthesis of strontium-titanate nanoparticles.[78]
	Silver nanoparticles (AgNP's) were prepared and used as antimicrobial agents. AgNP's were prepared by reduction of $AgNO_3$ by aqueous extract of the plant.[79]
Chemical composition	Acidic polysaccharides were isolated and identified (compared with *Malva sylvestris*).[80]
	Acidic polysaccharide, rhamnoglucouronan, was isolated from the stems of the plant and analyzed.[81]
	Phenolic acids (ferulic, vanillic, syringic, *p*-coumaric, *p*-hydroxybenzoic, *p*-hydroxyphenylacetic and caffeic) were identified and determined quantatively.[82]
	Partial chemical composition: some metals, amino acids and monosaccharides were identified and quantified.[83]
	Mercury accummulation in roots introduced compared with other plants in Poland.[84]
	Pictinic polymers (water and alcohol insoluble) from the flowers were isolated and analyzed to result mainly rhamnoglucogalacturonan, that consists rhamnose, glucorunic and galactorunic acids.[85]
	Two new compounds from ethanolic extract.[86]
	Isolation and identification of 17 known compounds.[87]
	Sono-assisted extraction of alcohol-insoluble compounds that yielded mainly high molecular weight polymers like peptides and polysaccharides (acidic).[88]
Antibacterial/Antimicribial/ Antifungal	Antimicrobial and cytotoxicity evaluation of *n*-hexane, ethanol, methanol, ethyl acetate and water extracts, against ten bacterial species and the fungus *Candida albicans*.[89]
	Ethanolic extract activity against nine bacteria species.[90]
	Water-ethanol (50%) extract found active against *Streptococcus pneumoniae* and *Klebsiella pneumonia*.[91]
Antioxidant	Antioxidant activity of methanolic extract (DPPH) with chemical analysis of phenolic compounds and saccharides.[92]
	Antioxidant activities of water, ethanol, butanol and chloroform extracts of the seeds were measured by three different methods and phenolic content was identified and quantified.[93]
	Aqueous mixture of polyphenols was force fed to rats and the animals were forced to swim to exhaustion. These animals showed longer swimming time compared to control. This was confirmed by tests of various metabolites.[94]
	Kaempferol and its 3-glucoside (astragalin) contained in ethanolic extract have strong antioxidant activity.[95]
Anticancer	Kaempferol and its 3-glucoside (astragalin) contained in ethanolic extract have strong anticancer activity.[95]
	Antiproliferative activity of methanolic extract against rat brain tumor and human cervix carcinoma cell lines compared with 5-florouracil and cisplatin (control).[96]
	Ethyl acetate seed extract inhibits the growth of stem cell driven colon cancer cells *in vitro* and antagonize the growth of tumor xenografts *in vivo*.[97]
Antiviral	80% Aqueous methanolic extract with anti-HIV activity.[98]
	Aqueous and ethanol extracts were tested for acyclovir-resistant Hsv type-1 in cell culture.[99]
Immunomodulatory	Aqueous extract is B-lymphocyte polyclonal activator.[100]
Urolithiasis preventive	70% Ethnaol/water extract prevented or reduced the formation of urinary tract stones.[101]
Cardiovacular protective*	Ethanolic extract of the flowers showed important preventive and curative effects of cariovasular disorders.[102] * See remark to this property after this reference.
Hepatoprotective	70% Methanol/water extract of the plant found active against acetaminophen-induced hepatotoxicity in mice. The systematic work included three control groups.[103]
Hypoglycemic	Ethanolic extract showed hypoglycemic activity and three new compound were isolated and characterized.[104]
Latex allergy prevention	Hospital staff were treated with 8% aqueous extract where the test group washed their hands with it before and after use of latex gloves.[105]
Tyrosinase inhibition	80% Aqueous ethanol inhibits the enzyme tyrosinase that is responsible for hyperpemintation of foods.[106]

The antimicrobial activity was also observed for few subspecies of *Alcea*. these reports are consistent. Ertas *et al*. reoprted in 2016 weak to moderate activity against different types of bacteia,[43] while Benli *et al*. stated that this subspecies had no antibacterial activity at all.[107] Despite the fact that this might seem contradicting, it is not: Ertas[43] used acetone while Benli[107] used methanol extract. When Ertas used methanol, no activity was observed. This may indicate that the active compound(s) that has the antimicrobial activity that was reported by Ertas, can not be extracted by methanol, possibly due to its high polarity of this solvent. So, further studies are needed, using not only both the solvents, but also other solvents like n-butanol, since using either very polar (water, Ertas) or non-polar (petroleum ether, Ertas) extracts showed no activity. Qader and Awad tested the antimicrobial activity of the aqueous extract of *A. kurdica* and found it to be moderate.[52] This strengthens the need for extensive tests of antimicrobial activities for all *Alcea* subspecies, with as many solvents as possible. Strong antibacterial activity was reported by Esmaeelian *et al*..[55] They isolated the active compound from ethanolic extract and found it to be malvidin-3,5-diglucoside (Figure 1).



(**A**)



(**B**)

Figure 1. (**A**) malvidin-3,5-diglucoside (**B**) astragalin

These results were confirmed by later studies that investigated the antimicrobial activity of this compound present in other plants such as *Syzygium cumini*.[108] It is also consistent with the fact that malvidin-3,5-diglucoside is the dimethyl ether derivative of delphinin-3,5-diglucoside, an anthocyanin with strong antimicrobial activity.[109] The structures difference can also explain the higher activity of the free anthocyanin compared with the methylated form. The same active natural product was also tested for anticancer activity and showed positive results, separately or with cisplatin.[56] An interesting glucosylated polyphenol was isolated from *A. Nudiflora* is astragalin (Figure 1),[56] and its antimicrobial was discovered in later studies.[110] Relying on these and other findings, it is important to expand the search of such compounds in *Alcea* subspecies for antimicrobial testing.

In addition to malvidin-3,5-diglucoside and *A. nudiflora*, anticancer activity was reported only for *A. rosea*.[95,96,97] All the reported results indicate significant activities compared with well known anticancer agents such as cisplatin and 5-fluorouracil, where the anticancer activity of the plant material was higher than the later agent. These findings support the need for expansion of anticancer activity studies of other *Alcea* subspecies like *A. setosa*, which is very common on east Mediterranean region.

The antibacterial activity of *A. rosea* was reported by several groups. Mert *et al*.[89] studied the antimicrobial, cytotoxic and antifungal (*Candida albicans*) of four extracts of this plant. In this work, the ethanolic extract proved to be most effective. This extract was reported to have significant antibacterial activity against nine bacteria species, and only *Escherichia coli* was resistant.[90] This result is similar to the findings in the previous study. *Streptococcus pneumoniae* and *Klebsiella pneumonia* are also antibiotic resistant bacteria, but hydro-alcoholic exract of *A. rosea* seeds was effective against them.[91]

Unlike the antibacterial/antimicrobial activities of *Alcea* subspecies that have been reported in several publications, the antiviral activities of these plants have been studied rather poorly. Popov *et al*. do not specify whether an extract or a single compound that is responsible for the antiviral activity that they reported.[68] This makes their report hardly useful. Asres *et al*. found that the hydromethanolic extract has the potenial as an anti-HIV agent.[98] Despite the fact that aqueous and ethanolic extracts showed weak antiviral activity against acyclovir-resistant Hsv type-1 in cell culture,[99] this opens a window for further research in this area.

The bioremediation of heavy metal contaminated soils is an issue with growing concern, especially in the context of hi-tech massive use of these metals for different purposes, and specifically metals that are used in batteries production. *A. aucheri* was found as a promising plant for this task.[44] Two other *Alcea* subspecies were reported as heavy metal accumulators are *A. pallida* [64] and *A. rosea*,[83,84] and both were found to be less effective in accumulating heavy metals as compared to that by *A. aucheri*.

One of the notable indicators of the need of further investigations of the genus *Alcea* is the fact that the subspecies *A. digitata* was analysed only for families of some compound like phenolics, alkaloids and saponines.[45] Even though the same publication indicated the traditional uses of *A. digitata* (anti-inflammatory, mild cathartic), and a modern study indicates that its "compound" gave releif to cancer patients treated with radiotherpay, this "compound" is actually the plant powder.[46] At for the time of writing this article, the chemical coposition of *A. digitata* is completely unknown, and its potential therapeutic potential needs further studies.

Polysaccharide content of *Alcea* ssp. was among the first chemical analyses of these plants. Looking into the reports that cited here,[47,48,54,58,69,80,81,85] it is clear that acidic

polysaccharides are the dominant type. That is to say that uronic acids, mainly glucuronic and galactorunic acids are present in high concentrations. These natural produts have been reported to have various biological activities such as anticomplementary, hypoglycemic, antitumorial, diuretic and antidiarrheic.[111] Further studies of these polysaccharides are needed in connection with *Alcea* subspecies research.

In recent years there is a growing number of publications concerning acetylcholinesterase (AChE) inhibition activity, due to its importance in Alzheimer disease treatment. Synthetic drugs are being developed but notable efforts are being invested in the discovery of natural products that can be used for this objective.[112] Until the time of writing this article, two research article about this activity of *Alcea* genus as acetylcholinesterase inhibitorss were published. A significant activity was found for *A. kurdica*,[53] but activity was reported by Ertas *et al*. was very weak (butyrylcholineesterase).[43] Although it is clear that this genus has low content of alkaloids, which is the major known compound family responsible for AChE inhibition so far,[112] it is also known that other compounds can inhibit AChE, and more important, this inhibition can occur from synergism of natural products.[113] So, it is a clear need to study this activity of *Alcea* plants in depth, and possibly, in combinations with other plants.

Several authors,[59,60,61] have thoroughly investigated the polyprenol and other aliphatic content of *A. nudiflora*. It is interesting to see that different extracting solvents yielded different compounds and that the polyprenols are of the type shown in Figure 2.

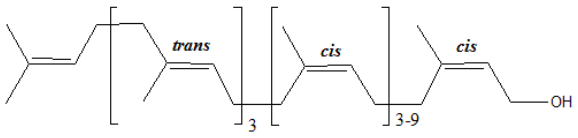


Figure 2. Polyprenols occurring in *A. nudiflora*

Interestingly, this general structure contains both geometries of the carbon-carbon double bond bond, cis and trans, unlike most naturally occurring polyprenols that contain one of these geometries.[114,115] These differences occur not only between species of different families, but within the same genus. A good and detailed example was published by Ertas *et al*.,[43] and details can be viewed there. But for interested readers, we bring here in table 4, the major compounds (in percentage terms) in the essential oils of *A. apterocarpa* and *A. pallida*. The phenolic compounds (ascorbic acid, caffeic acid, salicylic acid, p-hydroxybenzoic acid and quercetin) content was almost identical in both subspecies.

Azirak and Karaman[63] reported that among seven plants that they tested their resistance towards the allelopathy of essential oils extracted from ten different very common aromatic plants, only *A. pallida* showed full resistance. This research was cited by many later studies but this activity was never reported for other *Alcea* subspecies, and it might be interesting to test this. The test must include strong allelopathic plants like walnut (*Juglans* ssp.).

Table 4. Major constituents in the essential oils of the given species

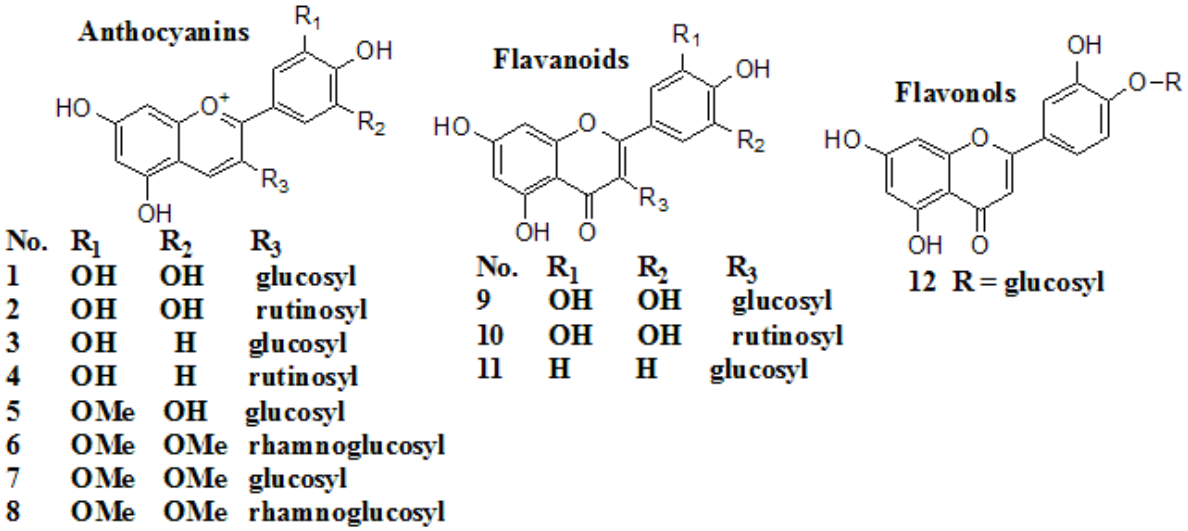
Compound	% in oil of *A. pallida*	% in oil of *A. apterocarpa*
α-Selinene	8.0	6.5
2,5-Ditertoctyl-p-benzoquinone	5.2	6.6
Arachidic acid	34.2	1.2
Hexadecanoic acid	6.6	1.0
Heptacosane	7.0	1.1
Nonacosane	6.3	1.1
Hexatriacontane	0.0	25.3
Tetratetracontane	7.0	15.4

In Table 3, medicinal/biological and other uses of *A. rosea*, a plant that thoroughly studied, are listed. In our opinion, other *Alcea* subspecies can be investigated in similar manner, especially the common ones such as *A. setosa*. One of the subjects that can be studied is the coloring and pigmentation of *Alcea* subspecies. As for *A. rosea*, it was sufficiently studied as can be seen in table 3.[75,76,77,78] These compounds are shown in figure 3.

It is interesting to notice some ambiguity in literature concerning the material named althaein.[75] While some publications consider it a mixture of glucosides,[116] others consider it the 3-glucoside of myrtillidin or petunidine.[117] Modern methods are being applied to identify and quantify antocyanins in plant matter.[118] The major advantage of these spectroscopic techniques is that they rely of fast sampling without needing long processing that can damage these relatively unstable compounds.

The isolation and characterization of two new and very interesting compounds shown in figure 4 below,[86] rises up the very basic fact that a complete chemical composition was never reported for any one of *Alcea* subspecies, especially *A. rosea*. The researchers named them "Rosea A" and "Rosea B" and the IUPAC names are given in the article.

Most efforts are still being targeted for studying the chemical composition of *A. rosea*, such as the recent work of Rakhmatova *et al*.,[87] who isolated seventeen known compounds viz., phytol, octanal, tetrahydrogeranylacetone, geranylacetate, farnesylacetone, menthone, acetylacetone, octacosane, stearyl alcohol, 2,5-dimethylfuran, isopulegol, α-tocopherol, α-tocopherylquinone, α-amyrin, β-amyrin, sitosterol, stigmasterol. In the same year, a report was published of new, very interesting compounds that were also isolated from *A. rosea* (Figure 5).[104] Therefore, further research work is required in this field since even partial chemical compositions of many *Alcea* subspecies is unkown.



No.	R_1	R_2	R_3
1	OH	OH	glucosyl
2	OH	OH	rutinosyl
3	OH	H	glucosyl
4	OH	H	rutinosyl
5	OMe	OH	glucosyl
6	OMe	OMe	rhamnoglucosyl
7	OMe	OMe	glucosyl
8	OMe	OMe	rhamnoglucosyl

No.	R_1	R_2	R_3
9	OH	OH	glucosyl
10	OH	OH	rutinosyl
11	H	H	glucosyl

Figure 3. Coloured compounds present in *A. rosea*

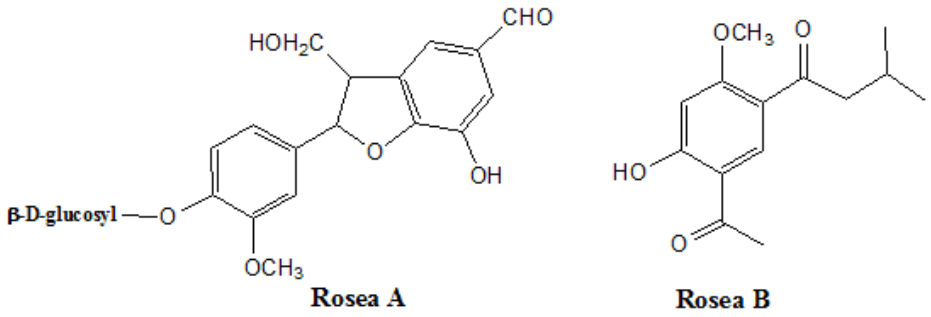


Figure 4. Compounds isolated from *A. rosea*

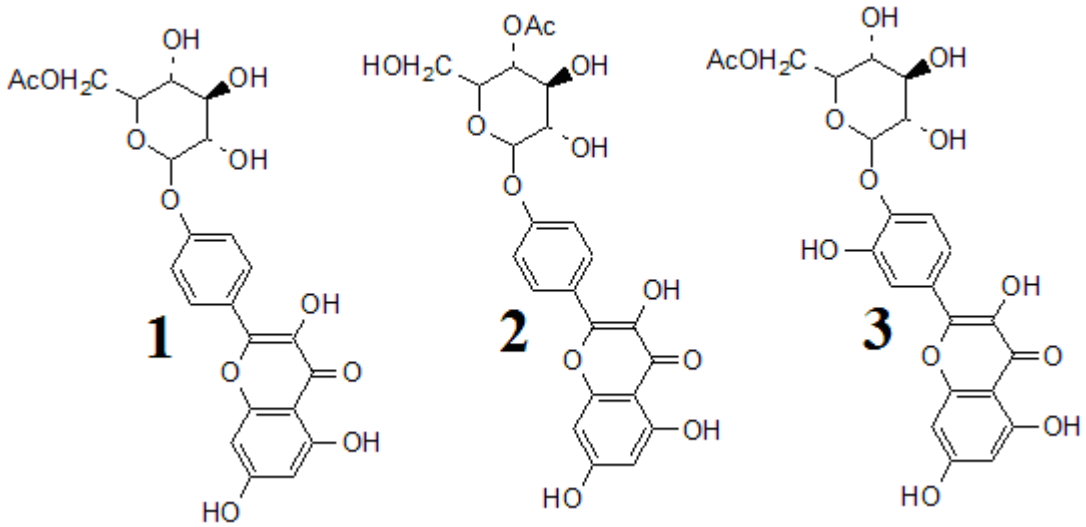


Figure 5. New compounds isolated from *A. rosea*

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Immunomodulatory activities related to *Alcea* were reported only twice until today.[61,100] In both these reports there are encouraging results but there was no followup research so far. And again, it is interesting why very common subspecies like *A. setosa* were not studied for this activity.

The last item in table 3, that reports the tyrosinase inhibition activity of hydroalcoholic extract of *A. rosea*,[106] is interesting because this article includes the same activity of three other plants, *Physalis alkekengi* L., *Bunium persicum* B. Fedtsch. and *Marrubium vulgare* L. Among these, *P. alkekengi* was the most active inhibitor of this enzyme that causes hyperpegmintaion, such as human skin and food browning, through catalysis of oxidative processes.[119] Efficient inhibition of this enzyme can be done by strong antioxidants. *P. alkekengi* and *A. rosea* contain considerable amounts of polyphenols, but *P. alkekengi* contains notable amounts of another antioxidant group of compound, steroids, which some of them were reported in the last decade.[120]

Finally, all activities reported in references 101 to 106 need extensive investigations for more *Alcea* subspecies.

Conclusions

Reviewing the scientific literature related to the genus *Alcea* that was published over almost five decades, it is concluded that

(a) The traditional uses of *Alcea* plants are well documented.

(b) The biological, medicinal and other activities of *Alcea* extend over a wide range, from direct use of the plant or its parts to nanochemistry.

(c) Only *A. rosea* has been well studied, but its complete chemical composition is still unknown and additional research is needed to explore its biological activities.

(d) For all other subspecies of *Alcea*, the chemical compositions are unknown and their biological activities were partially or very narrowly investigated.

(e) Few subspecies of *Alcea* were never studied for biological and other activities.

(f) The research of this genus is very far from completion.

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