# *AMARANTHACEAE* PLANTS OF ISRAEL AND PALESTINE: MEDICINAL ACTIVITIES AND UNIQUE COMPOUNDS

**Abdullatif Azab[a]***

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*Amaranthaceae* family is one of the largest and most diverse in the plant kingdom. While some of the plants of this family have important nutritional value, others are considered toxic and/or hazardous weeds and many efforts have been made in controlling them. But both categories were used by humans for traditional medicinal purposes, and some of them were extensively studied by modern science. In this review article, we will present some ethnomedicinal uses of the plants of this family, along with comprehensive literature survey of medicinal, biological and other activities. Information will be presented in tables for the convenience of readers, and many structures of natural products are presented. The extensive discussion section will focus mainly (but not only) on studies of active compounds production. This review article is about plants of this family in general and in particular about *Amaranthaceae* plants of our region. Conclusions and future research recommendations are also presented.

* Corresponding Authors
Fax: +972-4-6205906
Phone: +972-50-5650025
E-Mail: eastern.plants@gmail.com
[a] Eastern Plants Research Institute, Box 868, Arara, Israel 30026

## INTRODUCTION

*Amaranthaceae* plant family is one of the largest in the plant kingdom. This family is botanically considered part of the *Amaranthaceae-Chenopodiaceae* alliance, where the *Amaranthaceae* family includes ca. 69 genera and 1,000 species and the *Chenopodiaceae* includes ca. 100 genera 1,400 species.[1]

Archeological studies carried out in different locations suggest that *Amaranthaceae* plants were used by humans for various purposes. Las Canopas inhabitants used what the report authors refer to as *Amaranth* grains as food.[2] Despite the fact that specific species is not indicated, it is reported that these plants were domesticated and cultivated by these humans. They conclude that the plant species might be *Amaranthus hypochondriacus* or *A. cruentus*, with higher possibility of the second species. Rastogi and Shukla indicate in their comprehensive review article about human use of Amaranth plants that early archeological evidence shows that plants of this family were domesticated for nutritional uses, as early as 8000 years ago by Mayan civilizations.[3] Pre-Hispanic (1000-1550 AD) of Northwest Argentina, domesticated *Amaranthus caudatus* for food.[4] This conclusion was made based on isotopic (carbon and nitrogen) analysis of human remains found in that area. *Amaranthus retroflexus* grains were used as food, by humans who lived on the Eastern shores of the Mediterranean, in late Bronze age, 1550-1180 BC.[5]Another early evidence of consumption of Amaranth by humans was found in archeological studies in Mexico, where these plants were eaten around 4000 BC.[6]

Some of the domesticated plants of the *Amaranthaceae* family were modified and selected mutations proved to be very successful and widely cultivated by humans. For example, Quinoa (*Chenopodium quinoa*) is one of the healthiest grains, and its nutritional and economical importance is rising rapidly.[7] Spinach (*Spinacia oleraccea*) has been extensively studied, and its very high health benefits are well known.[8] Another domesticated species of this family, which was thoroughly studies, and has very high nutritional value, is Beet (*Beta vulgaris*).[9] Finally, some species on *Amaranthus* were domesticated for gardening and beauty purposes. A good example of these species is *Amaranthus tricolor*. Both domesticated and wild varieties of this species, are very beautiful and has notable medicinal and other biological activities.[10,11] But this review article, will focus only on wild species of the *Amaranthaceae* family that grow in Israel and Palestine. These are *Achyranthes aspera*, *Aerva javanica*, *Alternanthera pungens*, *Alternanthera sessilis*, *Amaranthus albus*, *A. blitoides*, *A. blitum*, *A. cruentus*, *A. graecizans*, *A. muricatus*, *A. palmeri*, *A. retroflexus*, *A. rudis*, *A. spinosus* and *A. viridis*.


**Figure 1.** *Amaranthus retroflexus*

**Table 1.** Ethnomedicinal and ethnobotanical uses of *Amaranthaceae* plants.

| Species, region | Region, uses, methods and references |
|---|---|
| *Achyranthes aspera* | India. Detailed review article about the many ethnomedicinal uses of this plant, with methods and plant parts. The publication presents some modern research findings.[12] This publication is titled "research article" despite being a typical review article. Less detailed than ref. 12, but it provides detailed presentation of folk medicine uses of the plant, according to rural areas people.[13]<br>Zambia. To treat HIV, cancer, pneumonia, cough, diarrhea, fungal infections of the skin and genital warts. Root infusion or whole plant decoction is administered orally, paste of the plant is applied to skin.[14]<br>Pakistan. Whole plant decoction, extract or powder are used to treat kidney stone, pneumonia, chest pain, puncture wounds, ulcer, dysmenorrhea, aerodontalgia and asthma.[27] |
| *Aerva javanica* | Skin diseases, headaches, wounds, injuries, snake bite, insect stings, malaria, kidney stones and bone fractures. Leaf paste is applied on the skin, or infusions are taken orally.[15]<br>Egypt. Roots and leaves are used to treat acne-like diseases and against "evil eye".[16] |
| *Alternanthera pungens* | Ghana. Leaves are ground and used for treatment of constipation and headaches.[17] |
| *Alternanthera sessilis* | Pakistan. Leaves juice or whole plant decoction, or cooked, are used for eye pain, galactagogue, leucorrhea, snake bite, diarrhea.[27] |
| *Amaranthus cruentus* | Pakistan. Eating cooked leaves has laxative effect.[18] |
| *Amaranthus graecizans* | Egypt. Leaves are used against constipation.[16] |
| *Amaranthus retroflexus* | Turkey. Leaves infusion is used for obtaining sterility.[21] Leaves are used as food.[22,23] |
| *Amaranthus spinosus* | Ghana. Whole plant is supplied as a decoction for treating malaria and fever. If crushed and used as a bath, it is used for baby refreshing.[17]<br>Pakistan. Dried seeds powder is taken orally with water to treat eye vision weakness.[19] Aerial parts extract to treat diarrhea, antidote, fever.[25] Whole plant decoction is used to treat gynecological disorders.[26]<br>Iran. This publication indicates the use of this plant in folk medicine but does not outline this use. It briefly presents some modern research results.[20] Leaves are cooked, squeezed for juice, extracted or prepared as decoction, to use for vermifuge, dyspepsia, diuretic, odontalgia, cataract, constipation.[27]<br>Tanzania. Leaves are cooked with milk for ulcer treatment.[24] |
| *Amaranthus viridis* | Pakistan. Dried seeds powder is taken orally with water to treateye vision weakness.[19] Leaves Extract, decoction, paste, are used to treat constipation, skin tonic, antidote, diuretic, cooking.[25] Whole plant decoction is used to treat gynecological disorders.[26] Leaves are extracted, powdered or prepared as a decoction, to treat painful urination, eye pain, constipation, piles, snakebite, cough andasthma.[27] Leaves or roots juice or decoctions are used to treat inflammations.[28] Leaves are crushed with sugar, mixed with tea to treat constipation. Extract is mixed with mustard oil to treat skin infections.[29]<br>Iran. This publication indicates the use of this plant in folk medicine but does not outline this use. It briefly presents some modern research results.[20]<br>Italy. Young leaves are used for pies.[30] |

**Ethnobotanical uses of *Amaranthaceae* family**

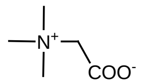
Many human societies have discovered the nutritional and medicinal potential of these plants since many millennia. But compared with other plant families, the published articles about the ethnomedicinal and ethnobotanical uses of *Amaranthaceae*, are few. Moreover, some species were not mentioned at all (6 *Amaranthus* species). In Table 1, these published reports are summarized.

While studying the published review articles about the plants of *Amaranthaceae* plants, we noticed that unlike most other plant families that were reviewed, in the case of this family, there are more review articles about single species, than about the entire family. This is one of the main reasons to write the present review article.

In addition to several review articles about ethnobotany and ethnomedicine of these plants (see previous section), a large number of articles have been published, presenting various properties, especially medicinal activities and chemical composition. The most important among them have been selected and their summaries are presented here.

***Achyranthes aspera***

This is the most studied and most reviewed of all plants of this family. One of the earliest review articles about this plant, is by Goyal and her colleagues.[31] It presents the known medicinal activities of the plant in folk medicine as well as modern research. It provides general chemical composition, and it its main importance is a table that presents the activities of different parts of the plant, their medicinal activities and active components (no structures), if known. Unlike that, the mini review article of Varuna *et al*., introduces a very limited scope of the medicinal activities of this plant.[32] It also provides very limited chemical composition, with one structure of Betaine (see Figure 2), with a minor error. There are several photos of the plant, but some of them are of very low quality.



**Betain**
**(Ref. 32)**

**Figure 2** Structure of Betaine, isolated from *Achyranthes aspera*.

Dey in his review article summarized enormous amount of scientific research and reports.[33] The article cites 265 publications, and it provides detailed chemical composition (no structures), and detailed presentations of botanical properties, traditional uses and reported medicinal activities of the plant. Compared with that, the review article of Shukla *et al* is highly valuable.[34] It contains detailed chemical composition, with structures of some important natural products, folk medicine uses and modern research reports, including highlighted antivenom activity. Among these natural products, there are few long chain alcohols (see Chemical Composition section). Tables are provided in the last pages of the article. There is one point that needs additional attention. Practically, there is no difference between sections 3 and 4. Both discuss chemical composition, despite having two different titles.

An excellent review article about *A. aspera* was published in 2011 by Srivastav and his colleagues.[35] It is comprehensive and presents all important aspects of this plant research, especially detailed chemical composition, with structures. The only weakness of this article is the detailed presentation of natural products names that occupied large space in the article, and were provided, anyhow, in the original research articles. On the contrary, the minireview of Hasan is very brief, does not present chemical composition and even the presentation of medicinal activities is very limited.[36] Photos of the plant are of low quality. In the review article of Srivastava, photos have high quality, chemical composition is extensively presented, medicinal activities are introduced, and traditional uses are mentioned.[37] There are two weakness points of this good review. First, many of the presented natural products have been isolated from other plants long time before detecting them in *A. aspera*, thus there was no need to show their structures. Secondly there is a mistake in the structure of Betaine, which is presented as an aldehyde, but it is an amino acid (see Figure 2).

In 2015, many review articles about this plant were published. Sharma and Chaudhary[38] presented the three major aspects of this plant (chemical composition, but no structures provided, ethnobotanical uses and modern research findings. They also presented a good comparison between traditional medicine and recent scientific medicinal activities. The minireview of Sureshkumar has the same structure.[39] The short minireview of Parmar and D. Sharma lacks ethnobotanical uses.[40] Ghimire and her colleagues published a large, good review article, in terms of chemical composition (some structures are presented) and modern research results of pharmacological activities.[41] It does not indicate ethnomedicinal uses.The review of Sanjay is disappointing. It looks like a copy of ref. 36 with exactly the same low quality photos.[42]

The review article of Vijayaraj and Vidhya, lists most of the active chemical components of the plant, presents many medicinal activities, but does not refer to folk medicine.[43] Anyhow, in our humble opinion, this article is of poor quality. It has two major weaknesses. First, the photos, which evidently were copied from other documents, have very low quality, including those that present chemical structures.

Second, the journal classifies the article as “review”, and the title of the publication is “Biological Activity of *Achyranthes Aspera* Linn. - A Review”, but in the introduction, there is a section titled “Collection and Authentication of Plant”, and a procedure for that is described. It is not clear why authors collected samples of the plant for writing review article. In the same year Saini published a very small review article about *A. aspera* that lists most of the active natural products, some of the published medicinal research articles, but did not relate to traditional medicine.[44]

Later in 2016, Verma published her review article.[45] This is a very short publication, that if informational part is extracted, it will not be more that two pages. But as far as we understand the term “review article”, even though its size is very small, this publication should not be named this way. It lists very partial chemical composition, does not mention traditional uses, cites only two publications (treatment of blindness and anticancer activity), and concludes that *Achyranthes aspera* L. (Latjeera) is a very important medicinal herb.

The size of the review article of Lakshmi and his colleagues is the same as ref. 45, three pages, but its quality is much higher.[46] After a short introduction, high quality photo, there is a brief presentation of major medicinal activity. Chemical compositions as well as traditional uses are indicated in brief. Another excellent review article was published in the same year by Rehman and her colleagues.[47] It presents all major aspects of interest about this plant. The two notes that should be given here are, first, there are many unnecessary common names, and, despite presenting detailed chemical composition, no structures were provided. Finally, the publication of Singh *et al*. is comprehensive and detailed for all aspects, but it lacks structures of important natural products that this plant contains.[48]

***Aerva javanica***

As far as our literature scan could reach, we found only two relevant review articles about this plant. First, the article of Vinit and Zaveri.[49] It focuses more on botanical studies, and lacks structures of important natural products, but the overall value of this article is high.But the review article of Payal and colleagues is low in quality.[50]

First, it is a 4 pages minireview titled “A Review on Phytochemistry and Biological Activities of *Aerva*”, but most of the article presents photos and botany of the plant. Second, the presented structure on Narcissin includes R group, without explaining what R stands for (L-rhamnosyl-β(1-6)-D-glucosyl-β-1- group). Third, the presented structures are of natural products contained in many other plants, while one of these natural products that were mentioned in the article, and contained only in the genus of *Aerva*, aervitin, was not presented (see Figure 3). Fourth, the presented structure of feruloyltyramine is wrong (see Figure 3).

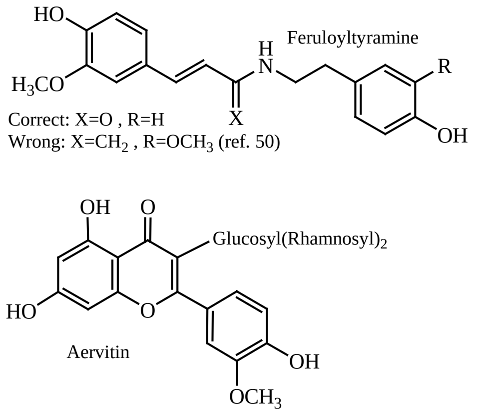



**Figure 3**. Structures of aervitin and feruloyltyramine

***Alternanthera sessilis***

Except for deserts and other arid landscapes, this plant is relatively widespread in the reviewed region, Israel and Palestine, but it is a typical fresh water-neighboring plant. The review article of Walter and his colleagues provides a limited view of this plant.[51] It presents botanical introduction, traditional uses, with a notable table that lists all Indian traditional medications (Siddha) that contain this plant or parts of it. But the presentation of modern research results is very partial. And the major weakness of this article is the presentation of the phytochemistry. The natural products that are introduced (β-Carotene and three natural phytosterols) are present in other plants in much higher concentrations and are not typical of this plant.

The review article of Laxmi *et al*., is misleading, the least to say but itcan be classified as scientific fraud.[52] It provides short botanical introduction, mentions chemical composition and some traditional uses, including for nutritional purposes. In this introduction, it cites 11 articles, including ref. 51 here. This is followed by the main part of that article, titled "activities reported of *Alternanthera sessilis*". Here the reporting is exactly as in research articles, including very detailed experimental procedures, and even plant collection and identification. No references cited in this section, and readers could be misled to think that this is an original article. The presentation of each activity includes all research steps, discussion and conclusions. It is not easy to believe that all these investigations were done in a single work. But the detection of misleading is quite easy: there are many mistakes of copying and pasting from original articles. For example, on page 3 of the article, page 2847 of the journal issue, there is a table titled "table 2". But the table was copied as an image from the original article of Kumar and Sanjib.[53] There, it appears as "table 1" (page 4), and Laxmi *et al*. did not pay attention to that numbering. Ref. 52 includes many other faults.

Rao focused in his review article on the botanical and ethnobotanical aspects of this plant.[54] The article mentions very briefly partial chemical composition (no structures) and few pharmacological activities. Contrary to that, the review article of Shehzad and his colleagues is of a high quality, comprehensiveness and photos.[55] Its only weakness is that it does not present unique natural products of this plant, and it does not present any chemical structures. The minireview of Chandrashekhar is satisfactory for this size article, but it lacks chemical structures of important active natural products.[56]

***Amaranthus cruentus***

This impressive plant annual, 70 cm high on an average, is very widespread in reviewed region (see Figure 1) and yet only one review article was found about it. The article of Wolosik and Markowska is of very high quality, despite having two weaknesses.[57] Its major strength is its comprehensiveness in terms of presenting the topics mentioned in the title. Its first weakness is that it focuses on big and macromolecules (fats, saccharides, amino acids and peptides), but almost ignores small molecules that are contained in the seeds and have notable medicinal activities. Secondly, the structures and the activities of the mentioned small molecules are not presented.

***Amaranthus palmeri***

Except for very dry areas, this plant is very widespread all over the reviewed region. It is immensely consumed by all plant eating animals. But despite that, only one review article was published about it by Ward and her colleagues.[58] This article focuses on the biological and agricultural aspects of this plant, and does not present traditional uses, medicinal activities or chemical composition. The only relation that it has to this section, is its high resistance to synthetic herbicides, such as the compounds shown in figure 4.

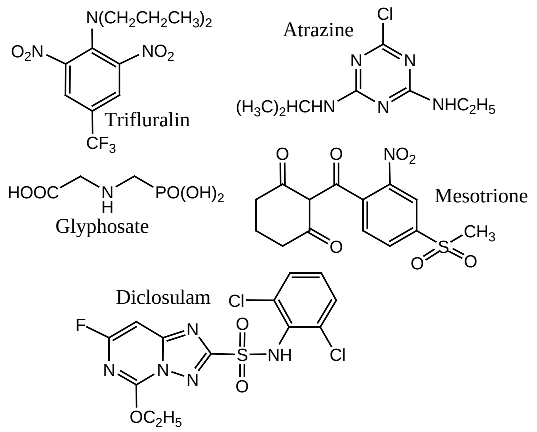



**Figure 4.** Herbicides that *Amaranthus palmeri* showed resistance to (ref. 58).

***Amaranthus spinosus***

It is considered invasive species in the reviewed region,[59] like all plants of *Amaranthus* genus, but *A. spinosus* is one of the most recent invaders, unlike some others (*A. rudis*), that invaded this region many centuries ago. It can be easily distinguished from other *Amaranthus* species, that all thrive in cultivated areas, since *A. spinosus* is spiny and painful if mistakenly touched.

The first review article that we present here about this plant, was published by Jhade and his colleagues.[60] It is comprehensive with wide medicinal activities presentation but limited in review of traditional uses and chemical composition. The review by Kawade and his colleagues, that was published 4 years later, has basically the same structure and size.[61] The traditional uses presentation is even smaller than in ref. 60, and the phytochemical section is slightly larger, but despite mentioning unique natural products to this plant (spinoside), no structures are presented. A very good review was published by Kumar and his colleagues.[62] It includes all expected and needed informational parts, with high quality photos and structure of unique natural products to this plant (Betanin and Amaranthine, Figure 5). It lacks a discussion section. And in the same year, Tanmoy and her colleagues published their review article.[63] It is comprehensive with structures of many natural products, but the images are vague and unclear. In addition, the traditional uses section is very small, but all other parts are satisfactory.

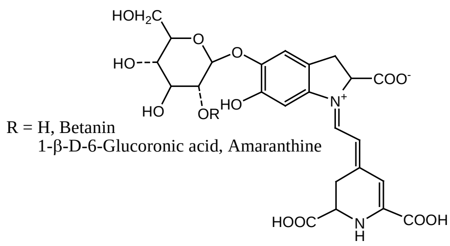



**Figure 5.** Betanin and Amaranthine isolated from *A. spinosus* (ref. 62).

Despite being properly written and arranged, we found the review article of K. Chandrashekhar, having low usefulness for readers that do not know Hindi.[64] The article have the requisite components needed for such a review, but tables 1 and 2 are meaningless for English readers. Since the journal is titled “International Journal of Ayurvedic Medicine”, and since the article is in English, translation of words from Hindi is totally inadequate. We are fully aware that such international articles can include some local common names, but not whole tables, which are supposed to be important parts of the text. Finally, the review article of Raut is superb. It is comprehensive, includes all needed components, well arranged, very useful tables and high-quality photos.[65]

### *Amaranthus viridis*

This plant is unmistakable, it grows around and in human habitats, flowering almost all year except for few cold weeks in the winter, has serrated dark green leaves with white coloring that has the leaf shape.

The minireview of Sowjanya and her colleagues about this plant is informational, satisfactorily written, but has three weaknesses.[66] First, the traditional uses part is very partial. Second, even though, the article is supposed to present “phytochemical and pharmacological potential” of this plant, the phytochemistry section is notably limited (one paragraph) and does not present structures of natural products. Third, the citation of literature is not appropriate. For example, in the paragraph of phytochemistry, the components of methanolic extract of leavesare presented and an article is cited. Directly after that, in the same paragraph, there is a brief description of the content of the roots of the plant and no reference is cited.

A year later, Ferdous and his colleagues published another minireview (that they titled as “comprehensive review”) about this plant.[67] It includes useful botanical information, relatively enough information about medicinal activities, high-quality photos, but lacks the parts of traditional uses and phytochemistry. Finally, the minireview of Singh and her colleagues provides very limited information about this plant, probably due to its small size (3 pages), and literature citation is poor, especially in the traditional uses part.[68]

### *Amaranthaceae* Family

M. Graca Miguel published an outstanding review about the family of natural compounds, Betalains, in the *Amaranthaceae* plant family.[69] But since this family includes many genera that some of them are not represented in the reviewed area, some vauable information presented in this superb review, is not relevant to our review. Anyhow, it presents this natural products family from different and comprehensive points of view. From this information, we present here the classification of Betalains, which is shown in Figure 6. So, Betanin and Amaranthine shown in Figure 5, are part of the Betalains subfamily of Betacyanins.

There are no published review articles for *Alternanthera pungens*, *Amaranthus albus*, *Amaranthus blitoides*, *Amaranthus blitum*, *Amaranthus graecizans*, *Amaranthus muricatus*, *Amaranthus retroflexus* and *Amaranthus rudis.*

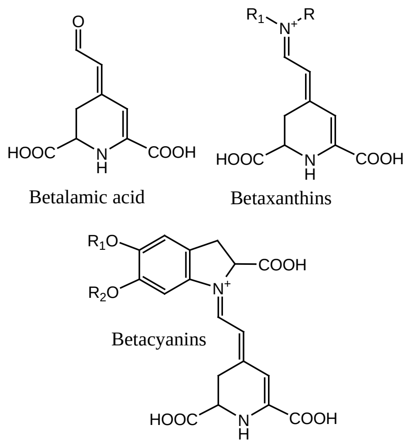



**Figure 6.** General structures of Betalains (ref. 69).

### *Amaranthus genus*

The review article of Alegbejo is informative regarding the species that the author chose to review.[70] But it is also confusing. In the abstract she states that “Amaranth consists of 60-70 species, 40 of which are considered native to the Americas”. Practically, this information is inaccurate: there are about 60 species native to America”.[71] Using any count, the author did not review most of these species. In addition, the author is from Nigeria, and she relate to traditional Nigerian medicinal uses of *Amaranthus*, that are not known to the traditional medicine of American peoples. The article lacks presentation of active ingredients and the traditional medicine part is very limited. Comparing with that, the review article of K. Peter & P. Gandhi is an excellent one.[72] It is very clear, highly informative with excellent figures. The only weakness of it is that traditional medicine and phytochemistry sections are very limited.

**Biological, chemical and other properties of *Amaranthaceae* plants**

When studying the published research literature about the plants of *Amaranthaceae* family that grow wild in the reviewed region, the result is quite interesting and not easy to understand. While some of these plants were extensively studies for almost every possible property, some others are completely missing in this type of scientific literature. These “missing” species are not particularly rare or highly toxic. We will refer to this fact in the discussion section.

So, to make it easier for scholars and interested readers, we summarized the published properties of each species in a separate table.

The data related to *Achyranthes aspera*, *Aerva javanica*, *Alternanthera pungens*, *Alternanthera sessilis*, *Amaranthus cruentus*, *Amaranthus graecizans*, *Amaranthus retroflexus*, *Amaranthus spinosus* and *Amaranthus viridis* are given in tables 2-10, respectively.

*Amaranthus blitoides*, in this interesting report, the allelopathic effect of this plant on common bean (*Phaseolus vulgaris*) was studied by three methods. First, the two plants were grown together. Second, shoots aqueous extract of *A. blitoides* was supplied to common bean seedlings, in greenhouse conditions. Third, active allelochemicals were extracted with ethanol from the aqueous extract, and they were administered to common bean seedlings. In all cases, the allelopathic effect was clearly observed.[255]

The general chemical composition of the plant with focus on antioxidants and minerals of *Amaranthus blitum* has been reported. Antioxidant capacity of ethanolic leaves extract was determined (DPPH) and its high value confirmed the high values of the antioxidant compounds concentrations.[256]

***Amaranthus muricatus***

This plant was very scarcely studied. Nutrients and antinutrients were determined in aerial parts before flowering.[280] General chemical composition was studied twice by the same research group.[281,282]

***Amaranthus palmeri***

This species was also very limitedly investigated. Water soluble organic compounds were isolated by solid-phase separation techniques, and they had slow, but clear allelopathic effect on onions and carrots.[283]A follow up study showed that volatiles (detailed GC analysis) that were released from aerial parts, had allelopathic effect on onion.[284]Since this plant has allergic effect on humans, a study revealed that the allergen in the pollen is profilin (14 kDa protein).[285] Finally, to the best of our knowledge, there are no publications that present novel natural products that were isolated from this plant, though the general chemical composition has been published.[286]

No research articles relevant to this review have been published regarding *Amaranthus albus* and *Amaranthus rudis*.

## DISCUSSION

After scanning the published literature about the *Amaranthaceae* plants of Israel and Palestine, the general but the very clear fact that arises is that some of these plants were extensively studied, while others were completely “ignored”. We have indicated this explicitly in the previous and main section of this review article.

The plant species of the family that was and still being most investigated is undeniably *Achyranthes aspera*. Evidently, the major mass of research and publication about this plant originate from India. Among the numerous medicinal properties of this plant, using its products as snakebite treatment is very notable. This use, as we have indicated earlier, is known in traditional Indian medicine and in modern research in this country. Based on the shocking, annual number of snakebite cases in this country, and even the more astonishing annual number of fatalities, 58000 in average,[401] it is very understandable why the use of this plant to treat snakebites is very common in India.

*A. aspera* is mentioned quite frequently in ethnomedicine literature of snakebite treatment,[402] along with modern research. But based on the availability of this plant (very widespread) and the number of deaths, this treatment needs very extensive research in order to make more effective.

The chemical composition of this plant was extensively studied, and in addition to know natural products, some very interesting compounds were isolated and characterized from its different parts (see Figure 7). But some of the reports about this chemical composition are misleading.

Generally, for the identification of a known compound in plant extract or essential oil, HPLC device and standards preparations are all what is needed. It is almost obvious that when detailed spectroscopic characterization is reported, they refer to a novel compound, which is not the case in some reports.[403]

In the previous section we have cited some reports of general chemical composition, and many more were published but we chose not to cite them. Here is another one.[404]

The *Achyranthes* genus is represented by a single species (among 16 in the world), *A. aspera*, and it is the same for the genus of *Aerva*, it is also represented by a single species (11 globally), *A. javanica*. This plant was moderately studied. But despite this, novel, interesting natural products were isolated from this plant (Figure 8). For this reason, there were many attempts to grow and cultivate it. In our region, anyhow, it’s a desert and arid regions plant, so it is not widespread but it is very well adapted to this habitat.[405]

**Table 2.** Biological, medicinal and other properties of *Achyranthes aspera*.

| **Activity/Property** | **Major Findings/Reference** |
|---|---|
| Analgesic and pain related activities | Aerial parts were extracted with methanol. The extract has analgesic activity in acetic acid-induced writhing test. [73] Leaves were extracted with 95% aqueous ethanol, and it proved antinociceptive in rat. Three pain-inducing methods were used: tail flick response, hot plate and formalin .[111] Roots were extracted with 95% aqueous methanol and extract (oral administration) was found antinociceptive in mice (acetic acid induced writhing).[112] |
| Antiallergy, skin protection, wound healing | Allergy was induced in mice by potassium dichromate and treated with methanolic whole plant extract. Positive results were recorded.[74] Seeds were extracted successively with petroleum ether, chloroform and methanol. Extracts found irritant to the inner surface of rabbit ear.[126] An ointment was prepared by using 5% leaves methanolic extract. This formulation was used to treat wounds (burn, wound) in healthy and diabetic (STZ-induced) mice. In both cases, the ointment showed clear wound healing activity.[128] Seeds were defatted with petroleum ether and extracted with 90% aqueous ethanol. Extract had wound healing activity (rats) in three tests: excision, incision, and burn wound.[129] |
| Antibacterial, antifungal, antiviral and related activities | Stem and leaves were separately extracted with chloroform, methanol, ethanol and ethyl acetate, to obtain 8 extracts. None of them had any antibacterial activity against 5 bacteria species.[78] Leaves and callus were extracted with ethanol, methanol, chloroform, benzene and petroleum ether. Contrary to the previous report, ethanol and chloroform extracts were active against all five species of tested bacteria, including *E. coli*, which ref. 78 reported no activity against it. All callus extracts except petroleum ether, were active against all bacteria species.[79] 70% Aqueous ethanol was used to extract leaves and shoots. This extract showed activity against 3 types of bacteria.[80] This interesting report, tested three variables. First, the yield of extraction of roots, stem, leaves and seeds, with hexane, ethyl acetate, methanol, ethanol and water; in three different months: January, May and September. Highest yields were in January. Second, antibacterial activity of these extracts against several bacteria species. Third, hexane stem extract was most active.[81] Trypsin inhibitor was isolated from seeds by standard protocol. It was tested and found active against 6 bacteria species and 4 fungi.[82] Stems and leaves were extracted separately with petroleum ether, chloroform, ethyl acetate, ethanol and methanol. All eight extracts were tested and found active against 3 bacteria species, except stem extracts that showed no activity against *Enterococcus faecalis*.[83] Used part of the plant was not indicated by authors, but in this important report, plant material was extracted with water, ethanol, methanol and chloroform. None of these extracts was successful antibacterial against all 6 species of multi-drug resistant clinical bacteria isolates, but none of them was completely inactive.[84] Leaves, roots, stemand flowers were extracted separately with petroleum ether, benzene, chloroform, ethyl acetate, ethanol and water. All extracts were partially active against cultured bacteria, but none was active against all species.[85] Aqueous extract of stems and roots was active against *Streptococcus mutans*.[86] Leaves were extracted with diethyl ether, ethyl acetate and acetone, separately. All extracts showed very mild activity against 2 bacteria species, but none was active against *Bacillus subtilis*.[87] Leaves and stems were extracted separately with petroleum ether, methanol, ethanol, ethyl acetate and chloroform. All extracts were active against 3 bacteria species, except stem extracts that were inactive against *E. faecalis*.[88] Methanol, chloroform and petroleum ether extracts of leaves were prepared, and tested against several species of bacteria and fungi. It is reported that (contrary to previous reports), only methanolic extract was active. In addition, extraction yields are notably low.[89] Acetone and aqueous extracts of leaves that were collected from different areas and mixed, were prepared. These extracts were active against 5 bacteria species. Extracts were analyzed for phenolic acids.[90] Seeds were extracted sequentially with chloroform, petroleum ether, acetone, methanol and water. All extracts had antibacterial activity against 8 bacteria species, except aqueous extract that had no activity against *Klebsiella pneumonia*.[91] This report is very interesting, since part of its result contradict most of previous cited reports. Leaves were extracted separately with water, ethanol and methanol and tested against 12 species of bacteria and fungi. All aqueous extracts were completely inactive, while other extracts had notable activity.[92] Whole plant methanolic extract was active against 4 fungi species.[93] Ethanolic leaves extract had notable activity against 3 fungi species.[94] 17-Pentatriacontanol (see Figure 7) was isolated from shoots, and it had activity against *Aspergillus carneus*.[95] Methanolic extract (plant part not indicated) was active against HIV viruses.[96] |
| Anticancer and related activities | Whole plant was extracted separately with petroleum ether, chloroform, ethanol and water. These extracts had cytotoxic activity (brine shrimp lethality), where aqueous extract was most active.[97] Roots were extracted separately with water and ethanol. Both extracts had anticancer activity against human colon cancer cells (COLO-2015). Aqueous extract had higher activity.[98] |

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| Antidiabetic, anti-obesity and related activities | Whole plant and methanolic extract were orally administered to normal and alloxan-induced diabetic rabbits. It both methods, significant lowering of blood glucose was recorded.[99] Leaves ethanolic extract had significant effect on STZ-induced diabetes in rats.[100] Plant commercial extract (part/s not indicated) had advanced inhibition of formation of glycation end products.[101] Leaves were extracted with 95% aqueous ethanol, and extract was successively fractionized with *n*-hexane, chloroform and *n*-butanol. All extracts were active against STZ-induced diabetes in rats, where positive controls were metformin and glybenclamide. In addition, four pure, known compounds that were isolated from extracts were tested and found active antidiabetic: oleolenic acid, ursolic acid, β-sitosterol and 17-triacontanol.[102] Herbal tea of leaves stems and flowers (combined) was prepared and administered to diabetic (alloxan-induced) rats. It had clear antidiabetic and hypolipidemic activities.[103] Ethanolic seed was supplied to diabetic rats (STZ-induced) and significant increase in blood glucose, as well as lower levels of blood lipids,were observed.[104] Saponin-rich fraction was obtained by extraction with 70% aqueous ethanol and 1-butanol, successively. This fraction has anti-obesity activity in high fat diet fed rats.[113] Powdered seeds were orally administered to high doses of fructose-fed female rats. Hypolipidemic effect was recorded.[137,138] Triton-induced hyperlipidemia in rats was treated with separately with aqueous and ethanolic leaves extracts. The alcoholic extract had significant effect, while the aqueous extract had none.[139] |
| Antioxidant, anti-inflammatory and related activities | Whole plant was extracted with methanol and extract was fractionized with several organic solvents. Saponin-rich fraction was found active against FCA-induced arthritis. FCA is mycobacteria.[76] Leaves were defatted with petroleum ether and extracted with water. The aqueous extract was active against formaldehyde-induced arthritis.[77] Seeds were extracted sequentially with chloroform, petroleum ether, acetone, methanol and water. All extracts showed antioxidant activity (DPPH), where methanolic extract had highest capacity.[91] Ethanolic seed extract was supplied to diabetic rats (STZ-induced) and significant decrease in the levels of superoxide dismutase and glutathione (GSH) peroxidase and increase in the levels of vitamin E, catalase, and reduced GSH were observed.[104] Ethanolic leaves extract was tested on carrageenan-induced hind paw edema and cotton pellet granuloma models in rats. In both cases, notable anti-inflammatory activity was recorded.[106] Roots ethanolic extract had anti-inflammatory activity in rats, that was observed in two tests: carrageenan-induced paw edema and cotton pellet granuloma.[107] Leaves and whole plants were separately extracted with water, and both extracts had anti-inflammatory activity in carrageenan-induced paw edema in rats.[108] Leaves were extracted with 80% aqueous ethanol, and extract had activity against inflammatory cytokines TNF-a and IL-5 in the lungs of mice.[109] In this important report, gel was prepared (procedure is provided) using aqueous roots extract. The gel was used to treat patients with chronic periodontitis and proved strong activity.[110] Methanolic extracts of leaves and roots were prepared and had high antioxidant activity (DPPH, ascorbic acid standard).[114] Stems were successively extracted with *n*-hexane, chloroform, methanol and water. Antioxidant was tested (DPPH) and methanolic extract had highest capacity. Oddly enough, authors report that extracts were tested against 4 bacteria species, and only *n*-hexane fraction was active against one species.[115] Leaves were extracted with 50% aqueous ethanol, and extract had high antioxidant activity (DPPH, NO radical inhibition).[116] Roots and flowers were extracted separately and sequentially with petroleum ether, benzene, chloroform, ethyl acetate, ethanolwater. General chemical composition of extracts was determined as well as antioxidant capacity (3 methods).[117] Leaves and stems were separately extracted with water, and extracts showed notable antioxidant (DPPH) capacity.[118] Ethanolic leaves extract was prepared, analyzed for general chemical composition, and tested for antioxidant capacity (phosphomolybdenum assay) was determined.[119] This study reports a comparison between the antioxidant capacity of *A. aspera* and *Cyathulaprostrata* that grow in Sri-Lanka. For both species, aqueous extract of whole plant was prepared, general chemical composition was determined, and antioxidant capacity was tested by four methods.[120] Whole plant was separately extracted with dichloromethane, ethyl acetate, methanol and water. All extracts were analyzed for detailed chemical composition, yet, no new compounds are reported. All extracts were tested for antioxidant capacity (4 methods).[121] Leaf aqueous extract was orally administered to rats, resulting reduction in liver lipid peroxidation and prothyroidic activity.[122] |
| Brain related activities | Aerial parts were extracted with methanol and theextract had CNS depressant activity tested by three methods.[73] Leaves were extracted with methanol and theextract showed anxiolytic activity. Authors refer this activity to the presence of alkaloids in the extract.[75] Roots were extracted with 95 % aqueous methanol and extract (oral administration) was found neuroprotective in mice (pentobarbital sleeping test, open field test).[112] Extracts and pure natural products from the plant were tested for nootropic activity (radial arm maze, step through latency in passive shock avoidance and increased recognition index). Results indicated modulating brain glutamatergic and cholinergic neurotransmission.[127] |

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| Cardiovascular system related activities | Leaves were extracted with 70 % aqueous methanol and extract was administered to mice. As a result, a significant increasein lymphocyte and platelet counts were recorded.[125] |
| Digestive system protection, hepatoprotection, nephroprotection, lung protection | Ethanolic and aqueous leaves extracts were administered to mice that had diarrhea induced by castor oil. Extracts had laxative as well as bronchodilator effects.[105] Roots were extracted with 95 % aqueous methanol and extract (oral administration) was found diuretic in mice.[112] Aqueous extract of roots prevented nucleation of calcium oxalate (urolithiasis) and preventing renal epithelial NRK-52E cells injury.[130] Leaves were extracted with petroleum ether, methanol, ethanol and water, but only ethanolic and aqueous extracts were used for *in vivo* studies. These extracts were orally administered to rats, and diuretic effect was recorded.[131] Whole plant was successively extracted with petroleum ether, chloroform, ethyl acetate, methanol and water. All extracts were tested for diuretic activity in rats, and methanolic extract was most active.[132] Aqueous extract of seeds had diuretic effect on mice and rats.[133] Leaves were extracted with 70 % aqueous ethanol and this extract had protective effect against pylorus ligation and chronic ethanol-induced ulcer in rats.[134] Whole plant was extracted with 50 % aqueous ethanol and this extract had protective effect against N-nitrosodiethylamine and $CCl_4$-induced hepatocarcinogenesis in rats.[135] Seeds were defatted with petroleum ether and extracted with 70 % aqueous ethanol. The extract had hepatoprotective activity against $CCl_4$-induced toxicity in rats.[136] |
| Enzyme inhibition, antivenom and related activities | Whole plant was separately extracted with dichloromethane, ethyl acetate, methanol and water. All extracts were tested for as enzyme inhibitors: AChE, BChE, α-amylase, α-glucosidase and tyrosinase.[121] Aqueous and ethanolic extracts of leaves were prepared and tested against snake (Ruselli's viper and Saw scaled vipe) in mice. This activity was tested by inhibition of venom phospholipase and procoagulant activity.[123] Aqueous extract of stems inhibited protease and phospholipase A2 from the venom of *Bitis arietans*.[124] |
| Insecticidal, molluscicidal, antiparasitic, herbicidal | Acetone and aqueous extracts of leaves that were collected from different areas and mixed, were prepared. These extracts had anthelmintic activity against *Caenorhabditis elegans*.[90] Various extracts and their combinations were used as herbicidal against 6 weed species. In all cases, positive results were recorded, and highest efficiency was found for fruit extract.[140] Leaves were extracted separately with acetone, chloroform, ethyl acetate, *n*-hexane and methanol. All extracts had moderate insecticidal activity against *Aedes aegypti* and *Culex quinquefasciatus*. A pure saponin that was isolated from the ethyl acetate extract, had strong activity[141] and it was identified as a compound that was isolated from *Achyranthes bidentate*, a species that is not included in this review.[142] Contrary to ref. 141, authors of this report published that leaves *n*-hexane extract had strong activity against *Aedes aegypti*.[143] Leaves and stems were separately extracted with *n*-hexane, and both extracts had significant activity against *Aedes aegypti*.[144] Aqueous extract of leaves had strong molluscicidal effect against *Biomphalari apfeifferi* and *Lymnaea Natalensis*.[145] Pure natural product (hormone) Ecdysterone (see Figure 7), that was isolated from ethyl acetate leaves extract, has strong activity against *Aedes aegypti*.[146] |
| Metals related activities | Methanolic leaves extract inhibited corrosion of mild steel that was exposed to industrial water medium.[147] Aqueous leaves extract was used to reduce silver ions ($AgNO_3$), to produce nanoparticles (AgNPs), which had notable larvicide against *Aedes aegypti*.[148] Aqueous leaves extract was used to reduce gold ion ($HAuCl_4$), to produce nanoparticles (AuNPs), which proved nontoxic, so authors conclude that they can be used for drug delivery.[149] Aqueous extract was used to prepare CuO nanoparticles, which had notable inhibition of cellular adhesion (*E. lenta* and *E. aerogenes*).[150] |
| Nutrition, toxicity | Leaves powder and their methanolic extract were fed to mice and no toxicity was recorded.[151] |
| Reproductive system, sex | Roots were extracted with 50 % aqueous ethanol and extract was orally administered to male rats. Results indicated reduction of sperm counts, weight of epididymis and reproductive system hormones.[152] Roots were successively extracted with petroleum ether, chloroform, ethanol and water. Chloroform and ethanolic extracts had antifertility activity in female rats.[153] Ethanolic extract of roots that was fed to pregnant female rats had 100 % combined antifertility activity (anti-implantation and abortifacient).[154] Leaves were extracted with 80 % aqueous methanol. This extract was administered to female rats, and it had combined antifertility effect, but it did not reduce reproductivity hormones.[155] Aqueous ethanol (50 %) was used to separately extract roots of *A. aspera* and *Stephania hernandifolia* (not included in this review). A composite of 1:3, respectively, was prepared and orally administered to male rats. The result was clear antifertility effect.[156,157] Roots were extracted with 50 % aqueous ethanol, resulting the isolation of 58-kDa protein. Its composition is not reported. This protein had clear antifertility activity. Gossypol was used as control antifertility agent in male mice.[158] A follow up study with the same protein, showed that it has antifertility effect on human males.[159] Similar study to references 156 and 157.[160] |

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| Chemical composition | Selected articles that reported general chemical composition, which means, natural products families (phenolics, carbohydrates … etc.), minerals or detailed chemical composition that included known compounds, without reporting novel natural products and their characterization.[161-168] First report of the isolation and the characterization of Ecdysterone from roots methanolic extract (Figure 7) that we mentioned earlier in ref. 146.[169] 36,47-Dihydroxyhenpentacontan-4-one (Figure 7) was isolated and characterized, from methanolic shoot extract.[170] A follow up study by the same research group resulted the isolation of two long chain compounds from the methanolic shoot extract, 27-cyclohexylheptacosan-7-ol and 16-hydroxy-26-methylheptacosan-2-one.[171] Two new saponins were isolated and characterized from the methanolic extract of aerial parts (Figure 7).[172] Futher analysis of the same extract, in a follow up study by the same group, resulted the isolation and characterization of three new saponins and two known compounds that were reported as new, but actually the are not (for example, Ecdysterone).[173] New cyclic chain fatty ether (interestingly, authors classified it as cyclic chain fatty acid) was isolated from the seed petroleum ether extract (Figure 7).[174] Even though new compounds were not reported in this study, an interesting and new method was developed for the determination of oleanolic acid in this plant.[175] New derivative (glucoside) of oleanolic acid was isolated and characterized.[176] Even though new compounds were not reported in this publication, it is very detailed, presents structures of active natural products and their GCMS chromatograms. This publication can be very useful.[177] Leave methanolic extract was analyzed by column liquid chromatography, and a new compound, aromadendrene-15-olyl ferulate was isolated and characterized (Figure 7).[178] Leaves were extracted and fractionized with several solvents. Fractions were analyzed resulting a new sesquiterpene (Figure 7) and other known compounds.[179] New 6-prenyl apigenin (Figure 7) was isolated and characterized from methanolic extract of leaves. This compound is candidate for developing novel monoamine oxidase-A inhibitor.[180] |

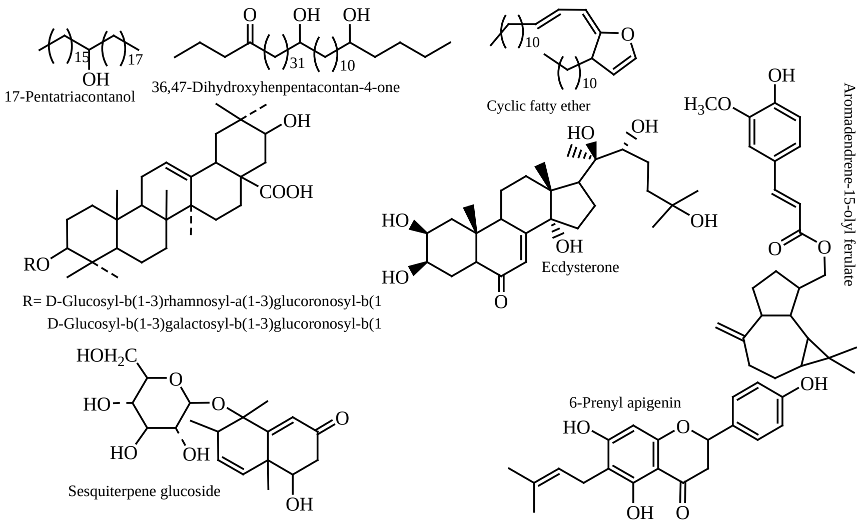


**Figure 7.** Active natural products isolated from *Aerva javanica.*

**Table 3.** Biological, medicinal and other properties of *Aerva javanica.*

| **Activity/Property** | **Major Findings/Reference** |
|---|---|
| Analgesic and pain related activities | Aqueous extract of leaves had antinociceptive (acetic acid induced writhing test, hot plate injury and tail immersion method) and antipyretic (Brewer's yeast induced test) activities.[181] |
| Antibacterial, antifungal, antiviral and related activities | Methanolic, ethyl acetated and petroleum ether leaf extracts were prepared and tested for activity against several species of bacteria and fungi. Methanolic extract was highly active, ethyl acetate extract had moderate activity and the non-polar extract was not active. Plant name is mistakenly written *Earvajavanica* instead of *Aerva*.[182] Whole plant was separately extracted with *n*-hexane, chloroform, ethyl acetate, methanol and water. Extracts were chromatographed and known active natural products were isolated. All extracts and natural products had weak to moderate antibacterial activity. Some of these compounds were isolated from this plant for the first |

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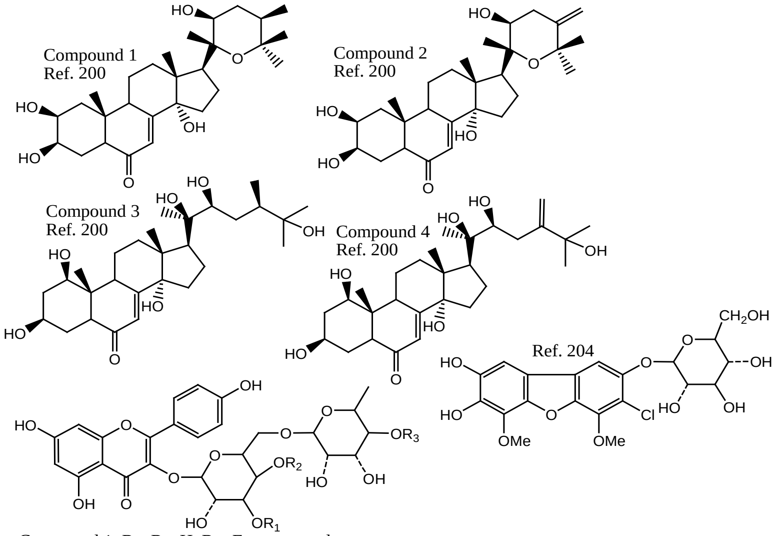
| | time.[183,184] Aerial parts were separately extracted with *n*-hexane, ethyl acetate, dichloromethane and methanol. All extracts were active against 5 bacteria species, where DCM extract was most active.[185] Whole plant was extracted with chloroform, ethanol and methanol. Extracts were tested against several bacteria species, and methanolic extract was most active.[186] Dried and fresh leaves were separately extracted with methanol, chloroform, petroleum ether, acetone or water. Each extract was tested against 4 bacteria species, and methanolic extract was most active.[187] Whole plant was extracted with acetone, ethanol, methanol and water, and essential oil was also prepared. All products were tested against several species of bacteria and fungi. Essential oil was most active.[188] Whole plant was extracted with 80 % aqueous ethanol, and extract was active against 6 bacteria species.[189] |
| Anticancer and related activities | Dried and fresh leaves were separately extracted with methanol, chloroform, petroleum ether, acetone or water. Each extract was tested against prostate and breast cancer cells, and methanolic extract was most active.[187] Whole plant was extracted with acetone, ethanol, methanol and water and essential oil was also prepared. All products were tested against human red blood cells. Ethanolic extract was the most active one.[188] Whole plant was extracted sequentially with *n*-hexane, chloroform and 80 % aqueous methanol. Extracts were tested against two human breast cancer cell lines (MCF7 and MDA-MB-231). Hydro-methanolic extract was most active.[190] Leaves were successively extracted with *n*-hexane, chloroform, ethylacetate, acetone, and methanol. Extracts were attested against human breast cancer cell line MCF7. All extracts had significant activities, where methanolic extract was most active.[191] |
| Antidiabetic | Leaf ethanolic extract had antihyperglycemic effect on alloxan-induced diabetes in mice.[192] |
| Antioxidant | Whole plant was extracted with acetone, ethanol, methanol and water, also, essential oil was prepared. All products were tested for antioxidant capacity (DPPH). Methanolic extract was most active.[188] Whole plant was extracted with 80% aqueous ethanol, and extract had high antioxidant capacity (DPPH).[189] Flowers were extracted with 50% aqueous ethanol, and extract was successively fractionized with petroleum ether, diethyl ether, ethyl acetate, benzene, acetone, and ethanol. Ethanolic and ethyl acetate fractions were used to test antioxidant (lipid peroxidation inhibition) in rats. Ethyl acetate fraction was more active.[193] Aerial parts were extracted with 70% aqueous ethanol, and antioxidant capacity (DPPH) of this extract was determined.[198] |
| Digestive system protection, hepatoprotection, nephroprotection, lung protection | Whole plant was extracted with 80% aqueous methanol and extract was defatted with*n*-hexane. The resulting crude solid was fractionized with water, dichloromethaneand ethyl acetate. Further fractionation and chromatography resulted the isolation of three known compounds. Fractions were tested for urease inhibition and found active, indicating anti-ulcer potential.[194] Aerial parts were extracted with 95% aqueous ethanol, and extract had activity against ethanol-induced gastric lesion in rats.[195] Whole plants was extracted sequentially with ethyl acetate and methanol. Extract had antilithiatic activity against ethylene glycol-induced hyperoxaluria in rats.[196] Whole plant aqueous and ethanolic extracts were active against castor oil induced diarrhea in rats.[197]Aerial parts were extracted with 70% aqueous ethanol, and this extract showed hepatoprotective activity against $CCl_4$-induced toxicity in rats.[198] The information in this publication is confusing. The title is “research paper”, which describes the hepatoprotective activity of whole plant extracts. Practically, it is written as review article.[199] |
| Enzyme inhibition | Flowers methanolic extract showed clear activity of the following enzymes inhibition: acetylcholinesterase (AChE), butyrylcholinesterase (BChE)and lipoxygenase (LOX).[200] |
| Herbicidal | Aerial parts aqueous extract had herbicidal activity against *Cyperus rotundus*.[201] |
| Toxicity | Aqueous infusions were prepared from aerial parts of female and male plants. These infusions were orally administered to female and male rats. At the dose of 500 mg $kg^{-1}$ for several weeks, female rats suffered hypochromic anemia.[202] |
| Chemical composition | Flowers methanolic extract was analyzed and four new compounds (Ecdysteroids, Figure 8) were isolated and characterized.200Chromatographic purification of ethyl acetate soluble fraction of the methanolic extractof the floweryielded three new acylated flavone glycosides(Figure 8).[203] A follow up study of the same extract by the same group obtained Aervfuraniside(Figure 8).[204] The following publications reported general chemical composition, and did not report new compounds: essential oil (stems and leaves) composition,[205] essential oil (seeds) composition, with comparison between methods of extraction,[206] composition of whole plant ethanolic extract,[207] very detailed and very useful analysis of various extracts of all parts, including mineral composition,[208] analysis of essential oils compositions resulting from transmission of phytoplasmas.[209] |




Compound 1: $R_1=R_2=H$, $R_3=$*E*-*p*-coumaryl
Compound 2: $R_1=R_3=$*E*-*p*-coumaryl, $R_2=H$
Compound 3: $R_1=H$, $R_2=R_3=$*E*-*p*-coumaryl

**Figure 8.** Active natural products isolated from *Aerva javanica.*

**Table 4.** Biological, medicinal and other properties of *Alternanthera pungens.*

| Activity/Property | Major Findings/Reference |
|---|---|
| Analgesic and pain related activities | Whole plant ethanolic extract was prepared and tested for analgesic activity in mice by hot plate test and acetic acid-induced writhing test.[210] |
| Antibacterial, antifungal, antiviral and related activities | Aerial parts were separately extracted with water, acetone, ethanol and petroleum ether. All extracts were tested for antibacterial activity and ethanolic extract was most active.[211] |
| Antioxidant, anti-inflammatory and related activities | Aerial parts were separately extracted with water, acetone, ethanol and petroleum ether. Antioxidant capacity of all extracts were determined by DPPH method.[211] Whole plant ethanolic extract was prepared and tested for antioxidant (DPPH) and anti-inflammatory (albumin denaturation technique) activities in mice.[210] Even though a detailed NMR work is reported, but the analyzed compounds are previously known phenolics. These were tested for antioxidant capacity (Trolox test). The report includes a confusing part (Extraction and isolation), where it states that aerial parts were extracted with "boiling ethanol", and when extract was concentrated, aqueous concentrate was obtained.[212] |
| Diuretic, gastroprotective | Whole plant ethanolic extract have diuretic effect in rats, like the effect of Furosemide.[213] Whole plant aqueous extract acted as gastro-stimulant in rats.[214] |
| Antiparasitic | Whole plant was successively extracted with n-hexane, chloroform, ethyl acetate and methanol. All extracts were tested for antiparasitic (*Pheritimaposthuma*) activity, and all extracts were active except methanolic.[215] |

**Table 5.** Biological, medicinal and other properties of *Alternanthera sessilis.*

| Activity/Property | Major Findings/Reference |
|---|---|
| Allelopathy, growth promotion | Aqueous extract of leaves was tested for allelopathic activity against seed germination of Rice (*Oryza sativa*). The allelopathic effect increased with concentration and when this reached 5 %, the germination of seeds was zero. Active phenolics in this extract are chlorogenic acid, gallic acid andvanillic acid.[216] Leaves were successively extracted with petroleum ether, acetone and ethanol. The ethanolic extract was fed to *Macrobrachium rosenbergii* (Prawn) resulting growth promotion in these animals. An excellent presentation of active natural products is provided.[217] |
| Analgesic and pain related activities | Aerial parts methanolic extract had analgesic activity in abnormal writhing test in mice.[218] Aerial parts were extracted with 90 % aqueous ethanol. Extract had analgesic activity in mice, as prove by two tests: acetic acid induced writhing test and hot-plate test.[219] Whole plant was defatted with *n*-hexane and extracted with ethanol, and this extract had antipyretic (yeast-induced) activity.[227] |
| Antiallergy, skin protection, wound healing | Aerial parts were extracted with 95 % aqueous ethanol and the extract had inhibitory effect in IgE-mediated allergicresponse in RBL-2H3 cells.[220] Leaves were successively extracted with petroleum ether, chloroform, acetone, methanol and water. All extracts (methanolic highest) had wound healing activity (excision, incision) in rats.[224] Stems were extracted with 90 % aqueous ethanol and extract had wound (scratch) activity.[225] |

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| Antibacterial, antifungal | Aerial parts were extracted with 95 % aqueous ethanol and extract was active against 6 bacteria and 3 fungi species.[222] Leaves were separately extracted with water, ethanol and acetone. Extracts and leaves juice had activity against 3 bacteria species.[223] Leaves were successively extracted with petroleum ether, chloroform, acetone, methanol and water. All extracts (chloroform highest) had weak to moderate activity against 4 bacteria species.[224] Leaves were extracted with methanol and petroleum ether, and both extracts were active against 3 bacteria and 2 fungi species.[226] |
| Anticancer | Aerial parts were extracted with ethanol, and extract had activity against human colon cancer cells (HT-29, 3T3).[228] |
| Antidiabetic, anti-obesity and related activities | Aerial parts methanolic extract had antidiabetic activity in glucose loaded mice.[218]Leaves were extracted with methanol and petroleum ether, and both extracts had antidiabetic activity (α-amylase inhibition).[226] Aerial parts were extracted with 95% aqueous ethanol, and extract was fractionized by *n*-hexane. This fraction was extracted with ethyl acetate, and the obtained extract antidiabetic activity in obese rats that had STZ-induced diabetes.[230] Leaves and callus were extracted with methanol, and extract was fractionized with several polar solvents. Extracts and fractions were tested for α-glucosidase inhibition. All showed notable activity, but callus extract was more active.[231] |
| Antioxidant, anti-inflammatory and related activities | Stems were extracted with 90 % aqueous ethanol, and its antioxidant capacity (DPPH) was determined.[225] Leaves were extracted with methanol and petroleum ether, and antioxidant capacity (DPPH) of both extracts was determined. Anti-inflammatory activity was proved by egg albumin test.[226] Leaves and callus were extracted with methanol, and extract was fractionized with several polar solvents. Extracts and fractions were tested antioxidant (DPPH) capacities.[231] Antioxidant capacities of ethanolic extracts of two cultivars of this plant, by three methods: DPPH, Trolox and FRAP.[232] Essential oil was extracted from aerial parts and its antioxidant capacity was determined by DPPH method.[233] Leaves were extracted with methanol and extract was fractionized with dichloromethane and *n*-hexane. Extract and fractions were tested for antioxidant capacity (DPPH).[234] |
| Brain related activities | Aerial parts were extracted with 90 % aqueous ethanol. Extract had stimulant activity in mice, as prove by three tests: Pentobarbitone-induced sleeping time test, open field test and hole cross test.[219] Methanolic extract of leaves had antidepressant (tail suspension and forced swimming tests) activity in mice.[229] |
| Cardiovascular system | Whole plant was extracted with 70 % aqueous ethanol and the extract was fractionized with water and dichloromethane. Extract and fractions had hypotensive effect in rabbits. Extract had higher activity than fractions[221] |
| Digestive system protection, hepatoprotection, nephroprotection, lung protection | Whole plant was extracted with 70 % aqueous ethanol and the extract was fractionized with water and dichloromethane. Extract and fractions had anti-asthmatic and anti-diarrheal effect in rabbits. Extract had higher activity than fractions[221] Aqueous extract of leaves had strong activity against castor oil-induced diarrhea in mice.[53] Ethanolic extract of aerial parts was active against damages in mice caused by three hepatotoxines: carbon tetrachloride acetaminophen and galactosamine.[235] Whole plant methanolic extract was active against damages in mice caused by carbon tetrachloride.[236] |
| Metals related activities | Aqueous extract of leaves was used as a reductant in the production of silver nanoparticles (AgNP's) from $AgNO_3$ solution. These AgNPs have antibacterial and antioxidant activities.[237] Young plants found active chromium ($Cr_2O_7^{-2}$) phytoremediator in,[238] domestic sewage,[240] PCB-contaminated soil (with an addition of Bentonite),[241] ions ($Cd^{+2}$>$Cr^{+3}$>$Pb^{+2}$). Antioxidant enzymes concentrations increased in different parts of the plant after absorbing the metal ions.[242] |
| Nutrition, toxicity | Leaves were analyzed for nutrients and antinutrients. Authors concluded that its safe and recommended to eat it.[243] |
| Chemical composition | Leaves were extracted with petroleum ether, resulting the isolation and characterization of a new natural product that authors symbolized with PDHC (Figure 9). Detailed structures of known compounds are also presented.[226] New saponin from methanolic extract of leaves(Figure 9).[244] Analysis of leaves ethanolic extract afforded new ionone (Figure 9).[245] Novel (plant defense) peptides were isolated from leaves aqueous extract.[246]The following references reported chemical compositions (some are very detailed) of known natural products.[233,234,247-250] Special method for detection and quantification of gallic acid in the plant.[251] Very extensive work was invested in this research, especially in spectroscopic characterization of the reported compound. Authors did not claim novelty, but the presentation of the work ("isolation and characterization") can mislead readers. Anyhow, this compound was isolated and characterized on year earlier.[252,253] Detailed work, including some useful chromatograms.[254] |

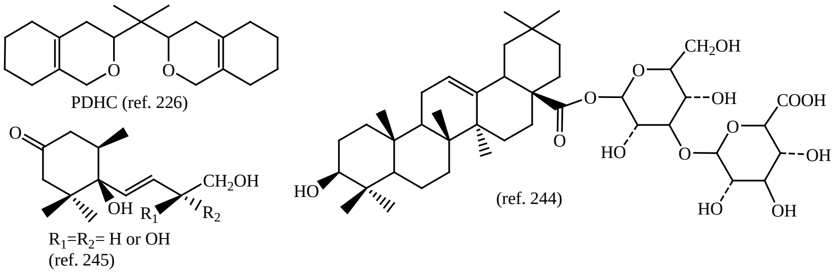


**Figure 9.** Active natural products isolated from *Alternanthera sessilis.*

**Table 6.** Biological, medicinal and other properties of *Amaranthus cruentus.*

| Activity/Property | Major Findings/Reference |
|---|---|
| Allelopathy | Tomato (*Lycopersicon esculentum*) was planted in soil that was brought from a field where *A. cruentus* was growing, shewed weak germination and growing compared to control.[257] Allelopathy of *A. cruentus* was clearly temperature-dependent, when its influence was tested by growing factors of several vegetables that were planted with *A. cruentus*. Influence was not uniform for all tested vegetables.[258] Aqueous extract of seeds had allelopathic effect on seedlings of garden cress (*Lepidium sativum*).[269] |
| Antihyperlipidemic | Seeds were defatted with *n*-hexane and hydrolyzed with pH=11 solution. Proteins contained in this hydrolysate, had inhibition activity of HMG-CoA reductase, suggesting possible hypocholesterolemic effect.[265] |
| Antioxidant | Seeds were extracted with methanol and the antioxidant capacity of this extract was determined by three methods (FRAP, DPPH and ABTS).[259] High fructose diet resulted in oxidative stress in rats. When co-administered with seeds, indications of decreasing malondialdehyde in plasma and increasing activities of antioxidant enzymes were recorded.[260] Aerial parts were extracted with 20 % aqueous acetone and the extract was fractionized with water. Antioxidant capacities of extract and fraction were determined by FRAP and DPPH methods.[261] |
| Blood related activities | Seed were separately extracted with *n*-hexane, ethanol and 70 % aqueous ethanol. All extracts had strong haemagglutinating properties.[262] Ethanolic extract of leaves had protective activity (aided in restoring the levels of red blood cells, white blood cells and hemoglobin) against phenylhydrazine-induced toxicity in rats.[263] Ethanolic leaves extract had hematopoietic effect on cyclophosphamide-induced toxicity in rats.[264] |
| Enzyme inhibition | Aerial parts were extracted with 20 % aqueous acetone, and extract was fractionized with water. Extract and fraction had xanthine oxidase inhibitory activity.[261] |
| Metals related activities | Analysis of seed samples that were collected from wild growing plants (USA), indicated high concentrations (accumulation) of toxic metal ions: $As^{+3}$, $Cr^{+3}$ and $Pb^{+2}$.[266] |
| Nutrition, toxicity | Major nutritional components of seeds flour and its protein concentrate were determined as phenolics, mineral, fatty acids and carbohydrates.[267] Dichloromethane extracts of seeds was found rich in saponin and toxic for hamsters.[268] |
| Chemical composition | Young methanolic extract of leaveswas analyzed resulting isolation and characterization of (*E*)-caffeoylisocitric acid (Figure 10). Its enzymatic synthesis is presented.[270] Novel pectinic polysaccharides were isolated and characterized from the methanolic extract of aerial parts.[271] The following publications presented interested information about chemical composition of the plant but did not report new natural products, HPLC method for isolation of betalains (Figure 6),[272] proteins and fibers,[273] HPLC method for analysis of phenolic acids and flavonoids in the seeds[274] and isolation of betacyanins (Figure 6) from the flowers.[275] |

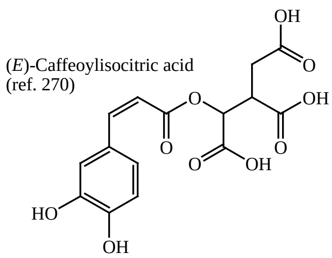


**Figure 10.** Active natural products isolated from *Amaranthus cruentus.*

**Table 7.** Biological, medicinal and other properties of *Amaranthus graecizans.*

| Activity/Property | Major Findings/Reference |
|---|---|
| Analgesic | Whole plant was extracted with 90 % aqueous methanol. This extract had analgesic activity tested by three methods (hot plate, tail immersion, acetic acid induced writhing) in mice.[276] |
| Antibacterial | Whole plant was extracted with chloroform, ethanol and methanol. Extracts were tested against several bacteria species and the methanolic extract was most active.[186] |
| Antioxidant, anti-inflammatory | Whole plant was extracted with 90 % aqueous methanol. This extract had anti-inflammatory activity tested by carrageenan-induced paw edema method.[276] Whole plant was extracted with methanol and extract was fractionized with water, *n*-hexane, chloroform, ethyl acetate and n-butanol. The antioxidant capacities of extract and fractions were determined by four methods: DPPH, FRAP, FTC and phosphomolybdenum. General chemical composition was determined in this study.[277] |
| Hepatoprotection | Whole plant was extracted with 90 % aqueous methanol, and extract was active against isoniazid and rifampicin-induced hepatotoxicity.[278] |
| Enzyme inhibition | Whole plant was extracted with 90 % aqueous methanol, and extract had cholinesterase inhibition activity.[276] |
| Chemical composition | Aerial parts were extracted with 10 % aqueous ethanol and the general chemical composition of extract was determined.[279] |

**Table 8.** Biological, medicinal and other properties of *Amaranthus retroflexus.*

| Activity/Property | Major Findings/Reference |
|---|---|
| Allelopathy | Aqueous extract of seeds had allelopathic effect on seedlings of garden cress (*Lepidium sativum*).[269] Leaves, stems and roots were collectively extracted with water, and this extract had allelopathic effect on Barley.[287] Whole plant aqueous extract had allelopathic effect on cucumber, alfalfa, common bean and bread wheat.[288] A follow up study by the same research group that tested the allelopathic effects of aqueous extracts on cucumber and wheat, but in this case, plant organs were extracted separately.[289] Plant powder had allelopathic effect on germination of maize.[290] |
| Allergy | Allergens were isolated from aqueous extract of pollen, and they were tested in human patients.[291] An allergen named Polcalcin was isolated from the aqueous extract of pollen. It can be produced in *E. coli*.[292] |
| Antibacterial | Leaves and flowers were combinedly extracted with 70 % aqueous ethanol and extract was active against 7 bacteria species.[293] |
| Antioxidant, anti-inflammatory and related activities | Leaves and flowers were combinedly extracted with 70 % aqueous ethanol and the antioxidant capacity of this extract was tested by DPPH method.[293] Leaves were extracted with 70 % aqueous ethanol, and this extract had high antioxidant capacity (DPPH).[294] Leaves were extracted with 10% aqueous methanol and 10 known nerolidol derivatives (structures are presented) were isolated and tested for their antioxidant capacities (DPPH).[295] |
| Metals related activities | Plant was found good phytoremediator of soil contaminated with $Cr^{+3}$, $Cd^{+2}$, $Cu^{+2}$ and $Ni^{+2}$.[296] Lead and zinc ions were successfully removed from wastewater, especially after treating the plants with growth promoter, citric acid.[297] Aqueous extract of leaves was used to reduce silver ions ($AgNO_3$ solution), to prepare silver nanoparticle, AgNPs, which had antifungal activity.[298] |
| Toxicity | Leaves were extracted with methanol-acetone-water (ratio is not indicated) and this extract was toxic only to renal cell culture.[299] Following cases of poisoning cases (renal) of livestock in Australia, aerial parts methanolic extract was prepared and analyzed. The major toxic ingredients were mainly quaternary ammonium and polyhydroxylated amines. New compounds were not reported.[300] |
| Chemical composition | Leaves were extracted with 10 % aqueous methanol and the extract was chromatographed, resulting the isolation and characterization of 7 new compounds that were identified as nerolidol derivatives (Figure 11).[301] A follow up study by the same research group afforded 4 new compounds from the same family, nerolidol glucoside derivatives.[302] An outstanding and comprehensive analysis of the chemical composition of the plant including a new natural product, a sphingolipid (Figure 11), has been reported.[303] Detailed composition of volatile compounds was analyzed from gases released by the plant itself, or from whole plant aqueous extract, that was subjected to vacuum distillation. New compounds were not reported.[304] Comprehensive analysis of water-soluble compounds, with special focus on carbohydrates, organic acids and phenolics was reported.[305] |

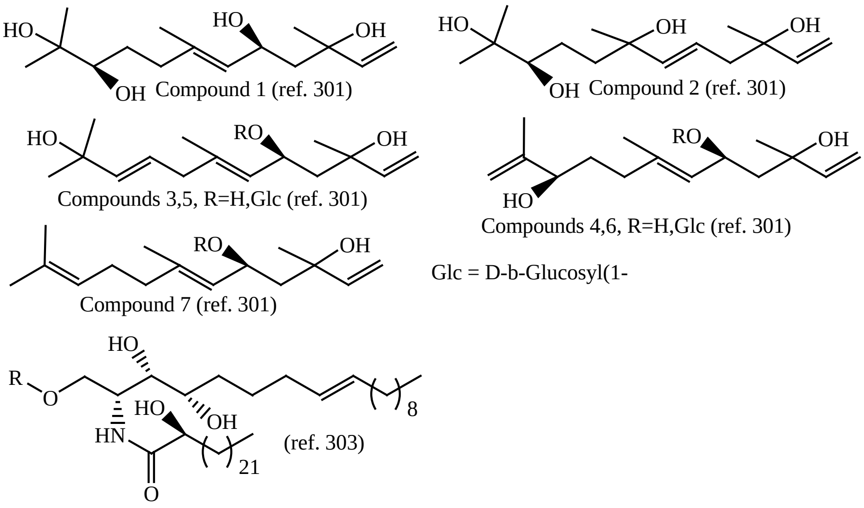


**Figure 11.** Active natural products isolated from *Amaranthus retroflexus.*

**Table 9.** Biological, medicinal and other properties of *Amaranthus spinosus.*

| Activity/Property | Major Findings/Reference |
|---|---|
| Allelopathy | Aqueous extract of leaves had allelopathic effect on the growth of mustard (*Brassica campestris*) and rice (*Oryza sativa*). This activity was also observed by inhibition of peroxidase, catalase and α-amylase activity.[306] |
| Allergy | Pollen was isolated from flowers and extracted with water. This extract was analyzed for proteins, and some of them had allergenic and antigenic activities.[307] |
| Analgesic and pain related activities | Whole plant was successively extracted with petroleum ether, ethyl acetate and methanol. Extracts had analgesic activity in mice, that was detected in two tests: acetic acid induced writhing andradiant heat tail-flick.[308] Whole plant was extracted with 50 % aqueous ethanol, and this extract had analgesic activity in rats, shown by four methods, formalin-induced pain, acetic acid-induced writhing, hot plate injury and tail immersion.[309] Leaves were separately extracted with ethyl acetate, chloroform, *n*-hexane, *n*-butanol and water. Ethyl acetate extract had highest analgesic activity in several (mentioned above) tests, in rats.[310] Leaves were extracted with methanol and extract had analgesic activity (mice) proved by the four methods.[318] Methanolic leaves extract had analgesic activity in three tests (mentioned above) in mice.[334] |
| Antibacterial, antifungal | Leaves were extracted with 80% aqueous methanol, and extract had activity against few bacteria species. General chemical composition has been presented.[311,312] Leaves were extracted successively with petroleum ether, diethyl ether, methanol and water. All extracts were active against five fungi species.[314] Whole plant was extracted with methanol and extract was active against rust disease. Very partial general chemical composition is presented.[315] |
| Anticancer | Whole plant was extracted with methanol and extract was fractioned with chloroform, ethyl acetate and *n*-hexane. From the chloroform fraction, a fatty acid was isolated, and it had strong activity against HepG2 humanliver cancer cells.[316] Strangely enough, this acid is presented by authors in the title of the article as “A Novel Tetraenoic Fatty Acid”. But the same three authors, published the same acid (14E,18E,22E,26E)-methyl nonacosa-14,18,22,26-tetraenoate) as “A new ester of fatty acid”, one year earlier (see ref. 317). |
| Antidiabetic | Whole plant was extracted with methanol and extract was fractioned with chloroform, ethyl acetate and *n*-hexane. From the chloroform fraction, a new fatty acid was isolated and characterized (Figure 12). It had α-glucosidase inhibition activity.[317] |
| Antioxidant, anti-inflammatory | Whole plant was extracted with 50% aqueous ethanol, and this extract had anti-inflammatory (carrageenan-induced) activity in rats.[309] Leaves were separately extracted with ethyl acetate, chloroform, *n*-hexane, *n*-butanol and water. Ethyl acetate extract had highest antioxidant capacity (DPPH, $H_2O_2$). It had also anti-inflammatory activity against inflammations that resulted from analgesic activity tests, in rats.[310] Leaves were extracted with 80 % aqueous methanol and antioxidant (DDPH) capacity of extract was determined.[311] Leaves were extracted with methanol and extract had anti-inflammatory activity in mice, tested by carrageenan-induced inflammation.[318] Roots were successively extracted with petroleum ether, ethyl acetate and methanol. The antioxidant capacity of the three extracts was determined (FRAP, DPPH), and ethyl acetate was highest.[319] Ethyl acetate leaves extract had moderate antioxidant capacity (DPPH).[320] Antioxidant capacity of methanolic extract of leaveswas determined by four methods. Antipyretic activity of extract was tested by Brewer’s yeast test in rats.[321] In this comprehensive work, leaves were extracted with 80% aqueous methanol and distilled for |

| | |
|---|---|
| | essential oil. Both products were analyzed for chemical composition, and their antioxidant capacities were determined (DPPH, $H_2O_2$ and enzymatic assay). Detailed presentation of chemical composition is provided.[322] Methanolic extract of seeds had high antioxidant capacity (DPPH, $H_2O_2$).[333] Antioxidant capacity of leaves was determined by two methods (DPPH, $ABTS^+$). General chemical composition has been presented.[335] |
| Brain related activities | Leaves were defatted with petroleum ether and extracted with 95% aqueous ethanol. Extract had antianxiety activity which was induced in rats by several methods.[323] An earlier study by the same group, where whole plant was extracted with methanol and extract was tested for antidepressant activity, that was induced in rats by several methods. In both studies, acute toxicity and general chemical composition were presented.[324] |
| Cardiovascular system related activities | Leaves were extracted with 70 % aqueous methanol. When the extract was administered to rats, adverse effects of fat increasing in the plasma of rats were recorded. But when administered with ascorbic acid, a synergetic effect was observed.[325] Whole plant aqueous extract had toxicity only in high doses in rats, but its cardioprotective effect was weak and temporary.[326] |
| Digestive system protection, hepatoprotection, nephroprotection, lung protection | Leaves were extracted with methanol and extract had gastroprotective (gastric erosion assay) and antidiarrheal (castor oil–induced diarrhea) activities in mice.[318] Whole plant was extracted with 50 % aqueous ethanol. This extract had activity against castor oil-induced diarrhea and ethanol-induced gastric ulcer, in mice.[327] Leaves were extracted with petroleum ether, chloroform, ethanol and water. All extracts had anti-ulcer (pylorus ligation) activity in rats, where ethanolic extract was more active than others.[328] Whole plant was extracted with 70 % aqueous methanol and extract was fractionized by ethyl acetated and water. Three animal species were administered with carbachol and treated with extract and fractions. These had bronchodilator andgut modulatoryactivities, where extract was more active than fractions.[329] Whole plant aqueous extract had diuretic activity in rats.[330,331] Whole plants was extracted with 50 % aqueous ethanol and this extract had activity against d-galactosamine/LPS-induced hepaticfailure.[332]Seeds methanolic extract had activity against hepatotoxicity associated with deltamethrin in rats.[333] |
| Insecticidal | Whole plant was extracted with 70% aqueous ethanol. This extract combined with the same extract of *Andrographis paniculate* were active against*Plasmodium berghei*-infected mice.[336] |
| Metals related activities | Leaves ethanolic extract was used to reduce $Au^{+3}$ ions ($H_4AuCl_3$) to prepare gold nanoparticles, AuNP's.[337] Aqueous leaves extract was used to prepare FeO-NPs from $FeCl_3$ solution.[338] |
| Nutrition, toxicity | Aerial parts were successively extracted with *n*-hexane, chloroform, ethanol and water. Ethanolic extract showed toxicity in brine shrimp lethality test. Partial general chemical composition is presented. Interestingly, it is reported that none of these extracts had antibacterial activity.[313] Leaves were fed to *Clarias gariepinus* (African catfish species) as a potential protein source.[339] Consumption of aqueous extract of leaves by postpartum mothers, increased prolactin and breast milk.[340] Single report of poisoning as a result of consumption of the plant by sheep in Brazil. Various adverse physical damages were observed, but the major adverse effect was renal insufficiency.[341] |
| Reproductive system, sex | Roots were extracted with acetone, and extract was co-administered to male rats with acetone seeds extract of *Dolichosbiflorus*. Various adverse effects of on sex organ and enzymes were recorded.[342] Methanolic extract of leaves was co-administered with *Abrusprecatorius* extract (70 % aqueous methanol) to male rats, resulting increasing of infertility.[343] Whole plant ethanolic extract was orally administered to female rats, resulting contraceptive and abortifacient activities.[344] |
| Chemical composition | Analysis of whole plant methanolic extract (*n*-butanol fraction) afforded new natural product, Spinoside (Figure 12).[345] The following reports presented general chemical composition or known compounds, but they also presented uniqueness or special interest. Betacyanins and phenolics,[346] Very detailed composition with (or without) tables,[347-354] isolation of α-spinasterol from stem extract,[355] identification and quantification of quercetin in leaves extract,[356] isolation of mucilages from leaves[357] have been reported |

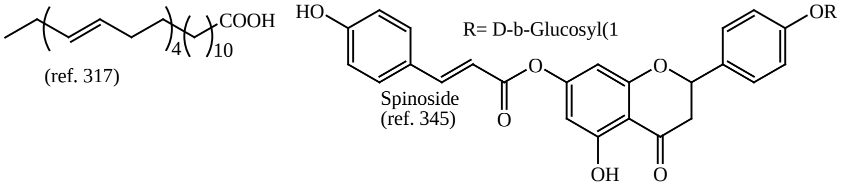


**Figure 12.** Active natural products isolated from *Amaranthus spinosus.*

**Table 10.** Biological, medicinal and other properties of *Amaranthus viridis.*

| Activity/Property | Major Findings/Reference |
|---|---|
| Analgesic and pain related activities | Methanolic whole plant extract had analgesic activity in three tests (mentioned above) in mice.[334] Whole plant methanolic extract of whole plant was had antinociceptive activity tested by acetic acid-induced writhing test, hot plate test and tail immersion test in mice. Antipyretic activity was tested by yeast-induced pyrexia method in rats.[365] Whole plant methanolic extract had antinociceptive effect against acetic acid-induced gastric pain in mice.[367] |
| Wound healing | Methanolic extract of leaves had wound healing activity (excision, incision, dead space) in diabetic rats.[366] |
| Antibacterial, antifungal | Whole plant was extracted with chloroform, ethanol and methanol. Extracts were tested against several bacteria species, and methanolic extract was most active.[186] Aerial parts ethanolic extract had activity against 5 bacteria and 5 fungi species.[358] Seeds (in the title it is indicated as leaves) methanolic extract was prepared and tested against 5 bacteria species. A GC-MS analysis is presented.[359] Extract of leaves alkaloids was found active against several bacteria species.[360] Seeds, leaves or aerial parts, were separately extracted with organic solvents, and extracts were active against some bacteria species.[361-363] Leaves were separately extracted with dichloromethane, ethyl acetate and ethanol. All extracts were active against two fungi species.[364] Analysis of seed extract (70 % aqueous methanol) afforded a new lectin that was active against two fungi species.[368] |
| Anticancer and related activities | Analysis of seed s extract (70 % aqueous methanol) afforded a new lectin that was active against HB98 and P388D1 murine cancer cell lines.[368] Leaves and stems were combinedly extracted with 50 % aqueous ethanol. Extract had activity against 3 human leukemic cell lines. General chemical composition is presented.[369] Leaves were extracted with *n*-hexane, chloroform, methanol and water. Methanolic extract had antigenotoxic activity.[377] |
| Antidiabetic and related activities | Whole plant methanolic extract had antihyperglycemic effect in glucose-loaded mice.[367] Whole plant was extracted with 75 % aqueous ethanol and the extract had activity against STZ-induced diabetes in rats.[370] Whole plant or methanolic extract of leaves had activity against alloxan/STZ-induced diabetes in rats, and antihyperlipidemic activity.[371,372] |
| Antioxidant, anti-inflammatory and related activities | Antioxidant capacity of methanolic extract of leaves was determined by two methods (DPPH and $ABTS^+$). General chemical composition is presented.[335] Various parts, were separately extracted with organic solvents, and extracts were tested for antioxidant capacities (DPPH).[361-363,374,375] Leaves and stems were combinedly extracted with 50 % aqueous ethanol, and the antioxidant (DPPH) capacity of extract was determined.[369] Whole plant methanolic extract had activity against lipid peroxidation in rats.[371] Leaves were analyzed for nutrient and mineral contents, extracted with methanol, and the antioxidant capacity of this extract was determined (DPPH).[373] Alkaloid-rich leaves extract had activity against $H_2O_2$ damage in human erythrocytes.[376] Leaves were extracted with *n*-hexane, chloroform, methanol and water. Methanolic extract had highest antioxidant capacity (5 methods).[377] Leaves, stems and seeds were extracted with methanol and the antioxidant capacity of each extract was determined by 5 methods. Anti-inflammatory activity was tested by hyaluronidase and lipoxygenase inhibition.[378] |
| Neuroprotection | Aqueous extract of leaveshad activity against cyclophosphamide-induced neuro-endocrine dysfunctiontoxicity in rats.[384] |
| Cardiovascular system related activities | Methanolic extract of leaves had hypocholesterolemic and anti-atherosclerotic effects in rabbits. Detailed HPLC analysis of extract is presented.[379] Leaves or whole plant methanolic extract had protective effect against isoproterenol toxicity in rats.[380,381] |
| Hepatoprotection, nephroprotection | Aquous extract of roots had activity against ethylene glycol-induced urolithiasis in rats.[382] Whole plant methanolic extract had activity against paracetamol liver toxicity in rats. Antioxidant biomarkers concentrations are reported.[383] |
| Enzyme inhibition | Leaves were extracted with *n*-hexane, chloroform, methanol and water. Methanolic extract had tyrosinase inhibition activity.[377] Leaves, stems and seeds were extracted with methanol and each extract had xanthine oxidase inhibition activity.[378] Phenolics rich aqueous extract of leaves, from cultivated plants, had trypsin inhibition activity.[385] |
| Metals related activities | Supplementation of FYM (farmyard manure) to cultivated plants, enhanced their ability as $Cd^{+2}$ accumulator.[389] Uptake of $Ni^{+2}$ inhibits growth of cultivated plants.[390] Plants have high tolerance to metal ($Cd^{+2}$, $Cr^{+3}$) soil contaminations.[391] Risk assessment of metals ($Cd^{+2}$, $Ni^{+2}$, $Pb^{+2}$) accumulation in plants, that grow in contaminated soil and can be consumed by humans as food, been reported.[392] Aqueous extract of leaves/twigs reduced $Ag^+$ ($AgNO_3$) for the preparation of silver nanoparticles, AgNPs, which had antibacterial sctivity.[393,394] |
| Nutrition, toxicity | Starch from this plant was modified (functional groups) for the purpose of using it as fat replacement.[395,396] Aqueous extract of leaves was not toxic to rats.[397] |

| | |
|---|---|
| Reproductive system | Aqueous extract of leaves had activity against cyclophosphamide-induced reproductive system toxicity in rats.[384] Roots powder had notable anti-menorrhagia in humanfemales aged between 16 - 45 years sufferingfrom excessive and or irregular vaginal bleeding.[386] Aqueous extract of roots had abortifacient effect in female rats.[387] Methanolic extract of leaves had estrogenic activity in female rats.[388] |
| Chemical composition | In addition to general chemical composition that was presented in previous cited publications, two more interesting articles did the same.[398,399] First isolation and characterization of Amasterol, an ecdysone precursor and a growth inhibitor (Figure 13).[400] |

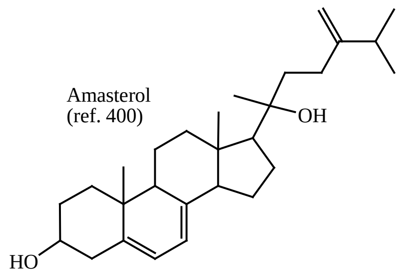


**Figure 13.** Active natural products isolated from *Amaranthus viridis.*

One of these notable attempts used the combination of Murashige and Skoog medium and indole acetic acid, as growth promoters. This research was performed for the aim of enhancement of active compounds production.[406]Another interesting cultivation used this plant to protect Cowpea (*Vigna unguiculata*) and Mung bean (*Vigna radiata*) crops from root rot fungi.[407]

*Alternanthera pungens* was very limitedly studied and most of its chemical and medicinal properties were not published (Table 4). Even its general chemical composition is still unknown and to the best of our knowledge, isolation of novel natural products from this plant has never been published.

On the contrary, the second representative of the same genus, *A. sessillis* has been well investigated and most of its properties are known and so is its chemical composition (Table 5, Figure 9). Some interesting natural products were isolated from that plant. But some of these cited reports seem confusing when the information that they include are compared. Lalitha Sree *et al*. state that leaves of this plant are highly nutritional, and it is safe to consume them.[243] Singh and her colleagues go even beyond that: they consider it a famine food plant and report its cultivation under different growth promoting conditions.[408] But Gayathri *et al.* reported three years earlier that aqueous extract of aerial parts was found hepatotoxic in mice.[409] Finally, it is important to include into toxicity considerations not only the location of the plant harvest and soil contamination levels , but seasonal variations in the possibly toxic contents of the plant also.[410]

All other 11 plants of the *Amaranthaceae* family, that grow wild in Israel and Palestine, are of the genus *Amaranthus*. Many published articles present various aspects and properties of this genus, and we presented some of these publications earlier in this article. But some of these reports may need further examination.

One of these outstanding reports was published by Noori and her colleagues.[411]They analyzed aerial parts (excluding stem) of 7 *Amaranthus* (5 of them are included in this review article) species in Iran, for flavonoid content. Even though they did not report novel compounds, this work is very detailed, comprehensive and can be very useful for interested researchers and scholars. An early review article by Suma *et al*. focuses on the allelopathy of some *Amaranthus* species.[412] It's a useful publication, but it needs updating and despite including a section of allelochemicals, no structures are presented, and it is very brief. Finally, an important work was published by Srivastava, about the nutritional potential of some cultivated wild *Amaranthus* plants.[413] The importance of this work emerges from the reported ability to cultivate these plants and to partially control their nutritional values.

The cultivation of *Amaranthus cruentus* drew notable attention from researchers and many works were published about this issue. Marin and his colleagues studied the influence of various cultivation parameters on seeds production due to their high nutritional value.[414] Kornarzynski and his colleagues reported growth promotion of this plant by electromagnetic stimulation to enhance the production of pigments (chlorophylls and carotenoids) in leaves.[415] Hlinkova and her colleagues grew this plant for two consecutive years and discovered high content of fatty acids (seeds) with notable unsaturation index (UI).[416]

As we mentioned earlier, *Amaranthus palmeri* also has not been investigated much. Its general chemical composition and its allelopathic effect on some domestic plants are partially known. Since in general it is considered a weed, its remarkable resistance to herbicides (see Figure 4 and ref. 58), like all *Amaranthus* plants, was studied.[417] Authors report that the plant has multiple resistance for 4 herbicides.

*Amaranthus retroflexus* is one of the most widespread *Amaranthus* plants in the reviewed region (Figure 1). It has been sufficiently studied (Table 8, Figure 11) and a remarkable number of very interesting, new natural products were isolated from this plant. In addition to the cited literature above, a special report about its chemical composition, was published by Woo.[418] This report indicated the very early scientific interest in this plant and its usefulness lies in the good graphical presentations of the chemical contents. The plant is mostly considered a weed and its resistance to herbicides is well known. Francischini *et al*. studied the resistance of this plant to acetolactate-synthase inhibitors, such as trifloxysulfuron-sodium and pyrithiobac-sodium (Figure 14),[419] and Wang *et al*. studied its resistance to thifensulfuronmethyland fomesafen (Figure 14).[420]

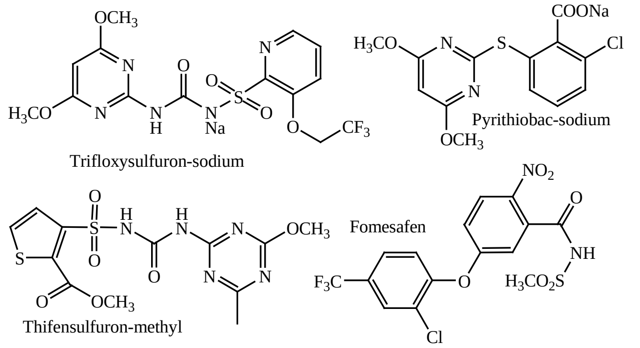


**Figure 14.** Herbicides that *A. retroflexus* showed resistance to (ref. 419, 420).

The toxicity of this plant goes way beyond allelopathy. An interesting study that was published by Dinu and her colleagues showed that the 50 % aqueous ethanol extract of leaves had toxic activity against mice, *Daphnia magna* (plankton) and *Triticum aestivum* (common wheat).[421] So, in addition to attempts of combating this plant with herbicides, some controlled cultivation trials were published, that aim to find the best method of preventing seeds germination,[422] including using growth promoters.[423]

The case of *Amaranthus rudis* is not quite understandable in terms of the lack of published studies about it. Its relatively not very common in the reviewed region as it grows only in the Northern parts of it but worldwide and especially in North America it is very widespread weed. This is probably the reason that the only publication, we found about it, is a study of its control by herbicides, in maize fields.[424]

*Amaranthus spinosus* is the most studied plant of the *Amaranthus* genus so far. Its medicinal properties and chemical composition (Table 9, Figure 12) are well known, especially the biologically active long chain alcohols. Its allelopathic effects are also known,[306,417] and so like other plants of this genus, several studies were performed about its control as a weed. One of these studies was carried out by Syahri and his colleagues where they tried a biocontrol method ofcontrolling *A. spinosus* using Mango leaf extract.[425] It should be noticed that the title of this publication stated that a “bioactive compound” was used, but actually its an extract not a pure compound.

*Amaranthus viridis* was also extensively (properties but very limited chemical composition) studied, but oddly enough, there are no significant reports about is allelopathy (Table 10, Figure 13). In many countries it is an invasive harmful plant to the local domestic and wild vegetation.[426] And like other plants of this genus, it has remarkable resistance to herbicides.[427] But despite that, in some regions in the world, it is cultivated mainly as a protein source.[428]

To conclude this part, we will cite two interesting reports related to *Amaranthus viridis*. First is the publication of Ratnasooriya and his colleagues about the lack of diuretic activity of hot water extract of whole plant of *Amaranthus viridis* L. in rats.[429] This work does not look obvious since generally such investigations are done to clarify, opposing, previous reports or to contradict unreliable reports. To the best of our knowledge, there are no publications that report diuretic activity of this plant, save in traditional medicine.[25]

Second, two new interesting natural products have been isolated and characterized, from *Chaetomium globosum*, a fungal endophyte isolated from *A. viridis* leaves (Figure 15).[430]

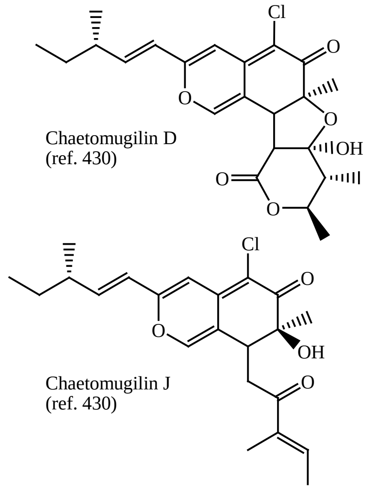


**Figure 15.** Novel compounds from *Chaetomium globosum*, a fungal endophyte isolated from *A. viridis* leaves.

## CONCLUSIONS AND FUTURE VISION

(1) Plants of the *Amaranthaceae* plants of Israel and Palestine, possess great properties. They contain unique natural products with special structural sub-units.

(2) Medicinal potential and properties of the plants is far from being fully explored. Most of the unique natural products isolated from these plants have not been studied yet for medicinal activities and their synthetic analogues have not been prepared and studied. Some of the species of this family have either limited studies or not at all.

(3) A very thorough study for the medicinal potential of these plants is needed. Efforts are needed to isolate new natural products from all the plants of this family. It is important to test the medicinal potential of these natural products. It is highly important to prepare synthetic analogues of these natural products and intensify the research of biocontrol of some of the species.

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## Personal notice from the author

I grew up in an agricultural family, and most local *Amaranthaceae* plants are very common in our fields and gardens. We have always known their allelopathic effects, especially that of *Amaranthus retroflexus* (Table 8). We unrooted them when they grew close to crops, but we highly esteemed them as food for our livestock. When I started the literature search for this article, a young plant of *A. retroflexus* started growing in our garden. So, I planted very young plant of Chile pepper (*Capsicum annuum*, *Solanaceae*) near it. Both plants grew very well, the plant of *A. retroflexus* started blossoming, but the pepper plant, despite reaching impressive size, was not flowering. I added flowering promoter to both plants, and *A. retroflexus* flowered more rapidly. The pepper plants were very green but no flowers or fruits. When *A. retroflexus* was about 100 cm high, I unrooted it. Within a week, the pepper plants were flowering so impressively and now (second week of August), they are heavily loaded with fruits.

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