colorMaker®

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January 15,, 2007

ORIGINAL

Robert L. Pooler
National Organic Program, AMS / USDA
STOP 0268 – Room 4008S
1400 Independence Avenue SW
Washington, DC 20250-0268

Re: Petitions for the Addition of
Non-Organic Agricultural Substances to the National List
Pursuant to Section 205.606 of the NOP

Dear Mr. Pooler:

Thank you for your letter, dated December 20, 2006, wherein you returned our original "combined" petition for fifteen natural colorants (dated October 16, 2006) and instructed us to file fifteen "separate" petitions, one for each colorant.

Pursuant to your instructions, please find enclosed with this letter fifteen (15) separate petitions, one for each natural colorant. We enclose an original and one copy of each petition for you to review. We ask the National Organic Standards Board (NOSB) to add onto the National List the following natural colorants:

Anthocyanins: (1) chokeberry juice, (2) black currant juice, (3) red cabbage extract, (4) purple carrot extract, (5) elderberry juice, (6) grape juice, (7) grape skin extract, (8) red radish extract; and

Carotenoids: (9) annatto seed extract, (10) beta-carotene from carrots, (11) lycopene, (12) paprika, (13) saffron; and

Betalains: (14) beet juice; and

Other: (15) turmeric.

You may recall that our original petition was organized by the four categories shown above. It may be prudent -- in the interest of time -- for the NOSB to consider the enclosed petitions in these same categories / groups.

Williamson
Color With Confidence

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5. The source of the substance and a detailed description of its manufacturing or processing procedures: Radishes grow underground throughout Asia and North America. The radishes are collected, washed, and cut into small pieces. The pieces are soaked in water. After 42 – 78 hours, the liquid is mechanically filtered and concentrated, producing a dark, blue-red liquid concentrate composed of the same anthocyanin molecules produced inside the radishes.

6. A summary of any available previous reviews by State or private certification programs or other organizations of the petitioned substance: No such government reviews of red radish extract are known; but anthocyanins (particularly from grapes) have been used since antiquity to color human foods and are Generally Regarded As Safe (GRAS).

7. Information regarding EPA, FDA, and State Regulations: FDA permits the use of red radish extract as a color additive exempt from certification. 21 CFR 73.260 Vegetable Juice. Red radish extract is also permitted as a natural color additive in foods in the European Union (E163) and throughout Asia.

8. The Chemical Abstract Service (CAS) number: There is no specific CAS Number for red radish extract; however, anthocyanins in general have been assigned CAS No. 11029-12-2.

9. The substance's physical properties and chemical mode of action: The anthocyanins extracted from radishes are distinct and unique molecules. They are different from carotenoids and betalains (other molecules used as natural colorants). Anthocyanins are sensitive to the pH of their surrounding environment, appearing red in an acidic pH (pH < 4.5.) and blue in an alkaline pH (pH > 6.5). In addition, anthocyanins display strong antioxidant properties which may be beneficial to human health. Beyond these unique properties, anthocyanins do not interact with substances used in organic food production and have no impact on the environment.

Radishes have been consumed for centuries and their growth and ultimate consumption has the exact same impact on the environment as organically grown, biodegradable fruits and vegetables.

10. Safety information about the substance: Please see the attached Material Safety Data Sheet (MSDS). Radishes, and the anthocyanins extracted from radishes, are GRAS.

11. Research information about the substance: See the attached Bibliography. A leading American researcher on anthocyanins is Professor Ron Wrolstad, Dept. of Food Science, University of Oregon, Corvallis, OR 97331. Dr. Worlstad recently retired, but he can still be reached at the University.

12(G) Justification Statements:

Enhanced Visual Appeal Using Natural Colorants. Food safety dictates that processed foods must be fully cooked to assure low bacterial counts for extended shelf-life and broad geographical distribution. Many food and beverage processors also employ a low pH environment and/or low water activity and/or or low temperature distribution of the finished product (refrigeration or freezing) to further assure minimal bacterial counts. These processing parameters are challenging to colorants residing inside the "core food" (for example, chlorophyll inside florets of broccoli, beta-carotene inside cut carrots, or anthocyanins inside strawberry preserves).

The addition of natural colorants compensates for the "original" colorants destroyed by high temperature / low pH processing. In so doing, the finished organic food or beverage product presents to the consumer the same visual appeal it would have if it were fresh. The addition of natural colorants can also enhance an existing color, making the organic food or beverage even more appealing; or it may extend the shelf-life of an organic food or beverage, making it available to more consumers both over time and geographical distance.

Without the addition of natural colorants, organic food and beverage products might lack the visual appeal and attraction of their direct non-organic competition. Thus, natural colorants help organic processors compete.

In so doing, natural colorants advance the organic philosophy by (literally) displaying to consumers visually appealing organic food and beverage products brightly colored without artificial colors such as FD&C Yellow 5.

Low Usage Levels of Natural Colorants. Because natural colorants are concentrated and very strong, they are used in organic food and beverage products at very low levels, typically less than 1%. The inherent strength of natural colorants sets in motion or "triggers" two distinct events: (1) natural colorants always fall under the 95 / 5 rule where five percent of the ingredients in an organic product may be non-certified; and (2) the volume of natural colorants purchased is very small.

By way of example, a hypothetical organic dairy develops organic certified yogurt. First, new product developers add red radish extract at 0.5% of the formula. They do not actively seek out organic certified red radish extract because they know the ingredient easily falls under the 95 / 5 rule. Second, the dairy's new product is successful and within the first year it produces 500 tons of organic certified yogurts. Despite such success, the dairy would purchase only 833 lb of red radish extract per month. This low volume of natural colorant sales, combined with inclusion of natural colorants in the "five percent non-certified" portion of the formula, provides little economic incentive to certify natural colorants as organic.

In the future, we anticipate the total amount of organic food and beverage products to increase. We may reach a point in time where a strong economic incentive places natural colorant crops under organic systems of production. It should be noted that no ingredient may remain on the National List for more than five (5) years without review by the National Organic Standards Board (NOSB).

The NOSB must therefore review the status of natural colorants five years hence (roughly 2012) and, at that time, may discover that an adequate supply of natural colorants is available for use in organic foods and beverages.

International Production of Natural Colorants. Most natural colorants are derived from International fruit and vegetable crops grown in developing countries; there is little International acreage certified organic. Most international organic acreage is utilized for corn, sugar and grains. Further, organic certification of International acreage remains problematic, plagued by cultural, financial, and language difficulties. Moreover, most fruit and vegetable crops are typically consumed where they are grown. As a result, there is a limited supply of the requisite fruit and vegetable crops needed for the creation of natural colorants.

Thus, natural colorants are not available in the appropriate quantity from International sources to meet the needs of organic processors.

Domestic Production of Natural Colorants / The Current State of the US Organic Industry. Certified organic cropland and pasture accounted for about 0.5% of total US farmland in 2005. Only a small percentage of top US field crops – corn (0.2%), soybeans (0.2%), and wheat (0.5%) – were grown under certified organic farming systems. Organic carrots (6% of the US carrot acreage), organic lettuce (4% of US lettuce acreage), and organic apples (3% of US apple acreage) were more commonly grown organic.

Markets for organically grown fruits and vegetables have been developing for decades in the US, and fresh produce is still the top-selling organic category in retail sales. Organic livestock was beginning to catch up with produce in 2005, with 1% of US dairy cows and 0.6% of the layer hens managed under certified organic systems. After decades of strong growth, the US organic marketplace is a bountiful "Farmers' Market" for consumers, but it does not supply the appropriate quantity of natural colorants for organic food processors.

Because there is no current supply of organic certified natural colorants from International sources, and because there is no current supply of organic certified natural colorants from US sources, and because natural colorants at levels below 5% greatly improve the visual appearance of organic foods and beverages, this Petition seeks the addition of natural colorants to the National List.

13. This Petition respectfully seeks the addition of red radish extract, a.k.a. "red radish," to the National List as a non-organic agricultural product under Section 205.606 of the NOP.

Respectfully Submitted,

COLORMAKER, INC.,
a California corporation

By: _____

Stephen J. Lauw
(Name & Title)

DD WILLIAMSON, INC.
a Kentucky corporation

By: Margaret A. Lawson

Margaret A. Lawson
(Name & Title)
VP Science & Innovation

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Hazard rating at a glance
0-least, 1-slight, 2-moderate, 3-high, 4-extreme

HEALTH	0
FLAMMABILITY	0
REACTIVITY	0

MATERIAL SAFETY DATA SHEET

1. *Product Identification:*

1.1 Product Name: Standard Red Radish Extract

1.2 Product Number: 2728C

1.3 Ingredient Statement: Red radish extract

1.4 Description of Product: A red liquid designed to color and function in food and beverage products. Specific formulation is withheld as a trade secret pursuant to 21 CFR 20.61. The characterizing principles and/or other components of this color blend are approved and are in compliance with 21 CFR 73. None of the ingredients appear on the list of hazardous items established under California's Proposition 65.

2. *Hazardous Ingredients and Exposure Limits:*

2.1 It is our opinion that the above named product does not meet the definition of a "Hazardous Chemical" as defined in 21 CFR 1910.1200. This MSDS is provided as general information for health and safety reasons.

3. *Health Hazard Data*

3.1	Carcinogenic	None known.
3.2	Acute Toxicity	None known.
3.3	Oral LD50	Not determined.
3.4	Dermal LD50	Not determined.
3.5	Ingestion	None known.
3.6	Skin Contact	None known.
3.7	Irritation (skin)	None known.
3.8	Irritation (eye)	May cause slight irritation.

4. *First Aid Measures*

4.1	Eye Contact	Remove contact lenses and flush eyes with copious amount of water for at least fifteen minutes. Contact physician if irritation persists.
4.2	Skin Contact	No significant health hazard. Wash exposed skin with soap and water for at least fifteen minutes. If irritation persists, consult a doctor.
4.3	Ingestion	Administer 1 - 2 glasses of water or milk to dilute. DO NOT INDUCE VOMITING. Seek medical attention if it seems advisable.

5. *Fire Fighting Measures*

5.1	Flash Point (method used)	Not determined.
5.2	Flammable Limits	Not determined.
5.3	Unusual Fire & Explosion Hazard	None known.
5.4	Extinguishing Media	Carbon dioxide, dry chemical, foam, and water spray.

6. *Spill, Leak, and Waste Disposal*

6.1 Absorb spills on vermiculite or other absorbent materials. Remove to approved disposal containers. Use rag and mop to clean small spots or dilute with large amounts of water. Colorant is biodegradable.

7. *Handling and Storage*

7.1 Store in a cool dry area. The wearing of rubber gloves and safety glasses to prevent skin and eye contact is recommended. Store in tightly closed containers.

8. *Exposure Protection*

8.1	Respiratory	No special equipment under normal conditions of use.
8.2	Skin	Skin protection appropriate to use conditions.
8.3	Eye	Safety glasses must be worn at all times
8.4	Hand	Suitable gloves.
8.5	Other	None

9. *Physical / Chemical Characteristics*

9.1	Appearance	Red liquid
9.2	Boiling Point	Not established
9.3	Vapor Pressure	Not established
9.4	pH value	7.0
9.5	Solubility in Water	Complete
9.6	Specific Gravity	To be established

10. *Stability and Reactivity*

10.1	Stability	Stable.
10.2	Incompatibility	Avoid strong oxidizing agents.
10.3	Hazardous Decomposition	Not known.
10.4	Hazardous Polymerization	Not known.

11. *Toxicological Health Hazards*

11.1 None known. Colorant is naturally derived and biodegradable.

12. *Ecological Effects*

12.1 None known. Colorant is naturally derived and biodegradable

13. *Disposal Considerations*

13.1 Incineration. Observe local, State, and Federal regulations concerning health and the environment. Do not incinerate in sealed containers.

The information contained herein is based upon data considered accurate and reliable. Nevertheless, an independent investigation and verification of this information should be made by the user. No warranty is made, expressed or implied, regarding the accuracy or correctness of these data. The use of this information and this product are beyond the control of ColorMaker, Inc. Therefore, it is the sole responsibility of the user to determine the conditions necessary for the safe use of this product.

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EVALUATION CRITERIA FOR SUBSTANCES ADDED TO THE NATIONAL LIST

Category 1. Adverse impacts on humans or the environment? Substance – RED RADISH EXTRACT

Question	Yes	No	N/A	Documentation (TAP; petition; regulatory agency; other)
1. Are there adverse effects on environment from manufacture, use, or disposal? [§205.600 b.2]		X		Petition; FDA regulations
2. Is there environmental contamination during manufacture, use, misuse, or disposal? [§6518 m.3]		X		Petition; FDA regulations
3. Is the substance harmful to the environment? [§6517c(1)(A)(i);6517(c)(2)(A)i]		X		Petition; FDA Regulations
4. Does the substance contain List 1, 2, or 3 inerts? [§6517 c (1)(B)(ii); 205.601(m)2]			X	
5. Is there potential for detrimental chemical interaction with other materials used? [§6518 m.1]		X		Petition; FDA Regulations
6. Are there adverse biological and chemical interactions in agroecosystem? [§6518 m.5]		X		Petition; FDA Regulations
7. Are there detrimental physiological effects on soil organisms, crops, or livestock? [§6518 m.5]		X		Petition; FDA Regulations
8. Is there a toxic or other adverse action of the material or its breakdown products? [§6518 m.2]			X	
9. Is there undesirable persistence or concentration of the material or breakdown products in environment?[§6518 m.2]		X		Petition; FDA Regulations
10. Is there any harmful effect on human health? [§6517 c (1)(A)(i) ; 6517 c(2)(A)i; §6518 m.4]		X		Petition; FDA Regulations
11. Is there an adverse effect on human health as defined by applicable Federal regulations? [205.600 b.3]		X		Petition; FDA Regulations

12. Is the substance GRAS when used according to FDA's good manufacturing practices? [§205.600 b.5]	X			Petition; FDA Regulations
13. Does the substance contain residues of heavy metals or other contaminants in excess of FDA tolerances? [§205.600 b.5]		X		Petition; FDA Regulations

1 If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

Category 2. Is the Substance Essential for Organic Production? Substance – RED RADISH EXTRACT

Question	Yes	No	N/A	Documentation (TAP; petition; regulatory agency; other)
1. Is there a natural source of the substance? [§205.600 b.1]			X	
2. Is there an organic substitute? [§205.600 b.1]		X		Petition
3. Is the substance essential for handling of organically produced agricultural products? [§205.600 b.6]			X	
4. Is there a wholly natural substitute product? [§6517 c (1)(A)(ii)]			X	
5. Is the substance used in handling not synthetic, but not organically produced? [§6517 c (1)(B)(iii)]	X			Petition; FDA Regulations
6. Is there any alternative substances? [§6518 m.6]		X		Petition; FDA Regulations
7. Is there another practice that would make the substance unnecessary? [§6518 m.6]			X	

1 If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

Category 3. Is the substance compatible with organic production? Substance – RED RADISH EXTRACT

Question	Yes	No	N/A	Documentation (TAP; petition; regulatory agency; other)
1. Is the substance compatible with organic handling? [§205.600 b.2]			X	
2. Is the substance consistent with organic farming and handling? [§6517 c (1)(A)(iii); 6517 c (2)(A)(ii)]	X			Petition; FDA Regulations
3. Is the substance compatible with a system of sustainable agriculture? [§6518 m.7]	X			Petition; FDA Regulations
4. Is the nutritional quality of the food maintained with the substance? [§205.600 b.3]			X	
5. Is the primary use as a preservative? [§205.600 b.4]		X		
6. Is the primary use to recreate or improve flavors, colors, textures, or nutritive values lost in processing (except when required by law, e.g., vitamin D in milk)? [205.600 b.4]			X	
7. Is the substance used in production, and does it contain an active synthetic ingredient in the following categories:				
a. copper and sulfur compounds;			X	
b. toxins derived from bacteria;			X	
c. pheromones, soaps, horticultural oils, fish emulsions, treated seed, vitamins and minerals?			X	
d. livestock parasiticides and medicines?			X	
e. production aids including netting, tree wraps and seals, insect traps, sticky barriers, row covers, and equipment cleaners?			X	

1 If the substance under review is for crops or livestock production, all of the questions from 205.600 (b) are N/A—not applicable.

CBI Deleted Version

Petition to the National Organic Standards Board and the National Organic Program for the Addition of Red Radish Extract to the National List Section §205.606

Item A

This is a petition to amend the National List Section §205.606 to include Red Radish Extract as a non-organically produced agricultural product allowed as an ingredient in or on processed products labeled as "organic".

Item B

1. Substance Common Name.

Red Radish Extract is the common name for the coloring components extracted from the scientific varieties of *Brassicaceae raphinus sativus.*

Other names: Red Radish Extract powder
Red Radish Extract concentrate
Red Radish Juice Extract

2. Manufacturers' Names, Addresses, and Telephone Numbers.

This petition is submitted by the International Association of Color Manufacturers' on behalf of our members.

International Association of Color Manufacturers'
1620 I Street NW, Suite 925
Washington, DC 20006
Phone: (202) 293-5800
Fax: (202) 463-8998

Contact: Sean Taylor, IACM Scientific Director
E-mail: staylor@therobertsgroup.net

Relevant member companies include (but are not limited to):

D.D. Williamson & Co., Inc.
1901 Payne Street
Louisville, KY 40206
USA

Wild Flavors, Inc.
1261 Pacific Avenue
Erlanger, KY 41018
USA

Chr. Hansen, Inc.
9015 West Maple Street
Milwaukee, WI 53214
USA

3. Intended or current use of the substance.

Red Radish Extract is a highly colored vegetable juice that has applications in food as a coloring substance. It is used to color a variety of organic and non-organic foods, including acidic foods, fruit preparations, ice creams, and jams and jellies. Red Radish Extract adds a red or pink color to foods, depending upon the exact concentration used. Red Radish Extract is generally used at a very low level in foods, with typical concentrations of 0.05-0.1% in the final food product. As is described in 21 CFR 73.260, Red Radish Extract is approved by the Food and Drug Administration (FDA) for use at all concentrations that are considered Good Manufacturing Practices and that do not exceed those levels necessary to provide the intended coloring effect.

Red Radish Extract is currently used as a color additive in a variety of organic and non-organic food products. In organic foods, Red Radish Extract has been in use as an allowed non-synthetic ingredient under "Colors, non-synthetic sources only," which is listed on the National List §205.605(a). However, the National Organic Standards Board has recommended that "Colors, non-synthetic sources only" be allowed to sunset off of the National List in October 2007. Therefore, Red Radish Extract must be added as an individual coloring substance onto the National List. Due to the minimal processing involved in its production, Red Radish Extract meets the current definition of an agricultural substance. This petition is to place Red Radish Extract as an allowed non-organic agricultural ingredient under §205.606 until such an organic form of Red Radish Extract is commercially available to organic foods producers in the necessary form, quality and quantity that is needed to fulfill the demands of the organic industry.

4. List of crop, livestock, or handling activities for which the substance will be used. If used for handling (including processing), the substance's mode of action must be described.

Red Radish Extract is used in handling only for food application as described above. The water-soluble extract is commonly added during formulation of the food product and it mixes homogenously with the aqueous phase. Red Radish Extract acts to supplement the inherent natural color found in the aqueous phase of the food product formulation. This natural color is often partially or completely lost during heating steps involved in the processing. As is described above, Red Radish Extract is used at very low levels in food products, and it therefore is not known to impart any other technical effect in the food product.

5. The source of the substance and a detailed description of its manufacturing or processing procedures from the basic component(s) to the final product. Petitioners with concerns for confidential business information can follow the guidelines in the Instructions for Submitting Confidential Business Information (CBI) listed in #13.

Red Radish Extract is the coloring material produced from the common red radish, *Brassicaceae raphinus sativus*. It is commonly available for use in coloring applications as either a powder or as a liquid. The common red radish grows naturally in all temperate regions and is eaten raw or cooked in many parts of the world.

CBI Deleted—processing information

CBI

6. A summary of any available previous reviews by State or private certification programs or other organizations of the petitioned substance.

To the best of our knowledge, no previous reviews have been conducted to approve the use of Red Radish Extract used as a food coloring material as a nonorganically-produced agricultural ingredient in or on foods labeled as 'organic' or 'made with organic'. Currently, all food coloring substances that are non-synthetic are on the National List, Section 205.605(a), under "Colors, Non-Synthetic Sources Only" (the NOSB was provided with a technical advisory panel review of "Colors, Non-Synthetic Sources Only" that was completed in October 2005. It is included as Attachment #1 to this petition). However, the National Organic Standards Board has recommended that 'Colors, Non-Synthetic Sources Only' not be renewed to the National List, and it is therefore scheduled to sunset from the National List effective October 22, 2007. Given this regulatory history, no state or private certification programs are known to have conducted reviews of Red Radish Extract.

Information about Red Radish Extract or other forms of red radish products sold as organic will be found in this petition. Please see Item B Nos. 11 & 12, Petition Justification Statement.

While to the best of our knowledge no other reviews have been Red Radish Extract, reviews of anthocyanins, the predominant coloring components in Red Radish Extract, have been done. They include the Summary of Evaluations Performed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). The evaluation of anthocyanins may be found at: http://www.inchem.org/documents/jecfa/jecmono/v17je05.htm and is included here as Attachment #2.

The Canadian Organic Standards, that were published September 2, 2006, include colors for use in food products under the following listing: §5.4.2.1 Colouring, natural, from non-synthetic sources only and shall not be produced using synthetic solvents and carrier systems or any artificial preservative.

7. Information regarding EPA, FDA, and State regulatory authority registrations, including registration numbers.

Red Radish Extract conforms in every aspect to the requirements mandated by the Federal Food, Drug, and Cosmetic Act. Red Radish Extract used as a coloring material is fully consistent with 21 CFR 73.260:

> Sec. 73.260 Vegetable juice.
>
> (a) Identity. (1) The color additive vegetable juice is prepared either by expressing the juice from mature varieties of fresh, edible vegetables, or by the water infusion of the dried vegetable. The color additive may be concentrated or dried. The definition of vegetable juice in this paragraph is for the purpose of identity as a color additive only, and shall not be construed as a standard of identity under section 401 of the act. However, where a standard of identity for a particular vegetable juice has been promulgated under section 401 of the act, it shall conform to such standard.
>
> (2) Color additive mixtures made with vegetable juice may contain as diluents only those substances listed in this subpart as safe and suitable in color additive mixtures for coloring foods.
>
> (b) Uses and restrictions. Vegetable juice may be safely used for the coloring of foods generally, in amounts consistent with good manufacturing practice, except that it may not be used to color foods for which standards of identity have been promulgated under section 401 of the act, unless the use of added color is authorized by such standards.

> (c) Labeling. The color additive and any mixtures intended solely or in part for coloring purposes prepared therefrom shall bear, in addition to the other information required by the act, labeling in accordance with the provisions of Sec. 70.25 of this chapter.
>
> (d) Exemption from certification. Certification of this color additive is not necessary for the protection of the public health, and therefore batches thereof are exempt from the certification requirements of section 721(c) of the act.

No listing for Red Radish Extract was found in the Environmental Protection Agency's (EPA) Substance Registry System (SRS).

Like all coloring materials, Red Radish Extract cannot obtain Generally Regarded as Safe (GRAS) status for its use as a color additive, and obtaining GRAS status for use as a color additive is not necessary. As is detailed in the Frequently Asked Questions (FAQ) section of the FDA's GRAS guidance website (http://www.cfsan.fda.gov/~dms/grasguid.html#Q6):

> Is a substance that is used to impart color eligible for classification as GRAS?
>
> The short answer is "No." Under section 201(s) of the Act, the GRAS provision applies to the definition of a food additive. There is no corresponding provision in the definition (in section 201(t) of the Act) of a color additive.
>
> However, under section 201(t)(1) and 21 CFR 70.3(f), the term color additive means a material that is a dye, pigment, or other substance made by a process of synthesis or similar artifice, or extracted, isolated, or otherwise derived from a vegetable, animal, mineral, or other source, and that is capable (alone or through reaction with another substance) of imparting color when added or applied to a food; except that such term does not include any material which FDA, by regulation, determines is used (or intended to be used) solely for a purpose or purposes other than coloring. Under 21 CFR 70.3(g), a material that otherwise meets the definition of color additive can be exempt from that definition on the basis that it is used or intended to be used solely for a purpose or purposes other than coloring, as long as the material is used in a way that any color imparted is clearly unimportant insofar as the appearance, value, marketability, or consumer acceptability is concerned. Given the construct of section 201(t)(1) of the Act and 21 CFR 70.3(f) and (g), the use of a substance that is capable of imparting color may constitute use as both a color additive and as a food additive or GRAS substance. For example, beta-carotene is both approved for use as a color additive (21 CFR 73.95) and affirmed as GRAS for use as a nutrient (21 CFR 184.1245); in some food products, beta-carotene may be used for both purposes.

8. The Chemical Abstract Service (CAS) number or other product numbers of the substance and labels of products that contains the petitioned substance. If the substance does not have an assigned product number, this fact should be reported.

Chemical Abstracts Service (CAS) No.:

528-58-5 (for cyanidin, the major anthocyanin coloring component in Red Radish Extract)
528-53-0 (for delphinidin, an anthocyanin coloring component in Red Radish Extract)
643-84-5 (for malvidin, an anthocyanin coloring component in Red Radish Extract)
134-01-0 (for peonidin, an anthocyanin coloring component in Red Radish Extract)
1429-30-7 (for petunidin, an anthocyanin coloring component in Red Radish Extract)
134-04-3 E163 (for pelargonidin, an anthocyanin coloring component in Red Radish Extract)

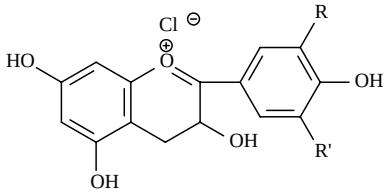
European Community (EC) No.:
E163 (for anthocyanins)

Color Index No.: None found

9. The substance's physical properties and chemical mode of action including (a) chemical interactions with other substances, especially substances used in organic production; (b) toxicity and environmental persistence; (c) environmental impacts from its use or manufacture; (d) effects on human health; and, (e) effects on soil organisms, crops, or livestock.

Red Radish Extract is an red/pink powder or liquid, depending upon the processing method. Red Radish Extract is soluble in water and mainly insoluble in ethanol and water. Although a variety of colored compounds are known to be present, the major coloring principles of Red Radish Extract are anthocyanins.

Anthocyanins are polyphenolic natural pigments that are widely distributed in the plant kingdom where they occur as glycosides (i.e., associated with a sugar moiety) in combinations that produce orange, red, blue, or purple coloration in a variety of fruits and vegetables. Commercial production of anthocyanins for use as coloring materials began roughly 30 years ago. They are obtained from edible fruits and vegetables, and traditional sources are black currant fruits, elderberry and black currant. The chemical structure of the most commonly occurring anthocyanins that are found in fruits and berries are shown below.



Cyanidin: R=OH, R'=H
Delphinidin: R, R'=OH
Malvidin: R,R'=OCH_3
Pelargonidin: R,R'=H
Peonidin: R=OCH_3, R'=H
Petunidin

Water-soluble anthocyanin pigments such as 3-mono-and 3,5-di-glucosides of malvidin, delphinidin and cyanidin, as well as their acyl ester derivatives, are responsible for the orange, red, blue, and purple colors of anthocyanin-containing fruits. The color intensity increases as pH falls, with stability being greatest below pH 4.5. Fruit extracts that contain anthocyanins are stable to light and temperature, but they are sensitive to oxygen, SO_2 concentration, and the presence of metal ions such as iron, tin, and aluminum which cause them to produce a bluer color (Marmion, 1991).

(a) Chemical interactions with other substances, especially substances used in organic production.

There are no reports of chemical interactions with other substances used in organic production of the food products in which Red Radish Extract is used as a coloring material.

(b) Toxicity and environmental persistence.

No relevant toxicity or environmental studies for Red Radish Extract were found. As anthocyanins are the predominant coloring pigments found in Red Radish Extract, data found for them is summarized below.

Genotoxicity

Anthocyanins are not genotoxic by a weight of evidence analysis (Brown & Dietrich, 1979; Ferguson *et al*., 1985; MacGregor & Jurd, 1978; Viola & Nosotti, 1978; Haveland-Smith, 1981).

Acute Toxicity

The extremely low acute oral toxicity of mixed anthocyanins (cyanidin, delphinidin, petunidin, and malvidin) is demonstrated by mouse and rat LD_{50} values greater than 25 and 20 g/kg bw, respectively (Pourrat *et al*., 1967). Welch's grape color extract administered to rats at 0, 5, 10, 15 and 20% of the diet produced no toxic signs or effects over the 30 day testing period (Stevens and Gallo, 1977).

Long-term Toxicity

No overt signs of toxicity were seen in rats given oral doses of 3000 mg/day mixed anthocyanins for 90 days (Pourrat *et al.*, 1967). No adverse effects occurred when dogs were fed a diet containing 15% grape color powder for 13 weeks (Becci *et al*., 1983a) or grape color extract for 90 consecutive days (Cox and Babish, 1978).

Reproductive/Developmental Toxicity

No adverse effects on reproduction occurred when grape color extract was fed to rats at dietary levels of 7.5 % and 15 % through two generations (Becci *et al*., 1983b; Cox and Babish, 1978). There were no teratogenic effects in multi-generation studies with rats, mice, or rabbits (Pourrat *et al*., 1967).

Metabolism

Anthocyanins are not readily absorbed from the intestine and the small quantity absorbed appears to be excreted by the kidney in its unchanged form (Horwitt, 1933).

Environmental persistence

There is no evidence of environmental persistence from the production of Red Radish Extract or anthocyanins used as a coloring material in foods.

(c) Environmental impacts from its use or manufacture;

There are no environmental impacts from the production of Red Radish Extract or its use in foods.

(d) Effects on human health

As described above, no studies have been conducted to gauge the genotoxicity, acute or chronic toxicity, or reproductive toxicity of Red Radish Extract. Red radishes have a long history of being used for human consumption, often raw but also cooked and in soups. No human health concerns have been noted through the use of red radishes in any of these products.

As noted above, preparations of red radish have very high concentrations of anthocyanin compounds. These naturally occurring antioxidants have been shown to be effective free radical scavengers in the body. The intake of natural antioxidants promotes general good health, and some evidence suggests that they reduce the risks of cancer, the neurodegenerative effects of aging, and the risks of developing cardiac diseases.

(e) Effects on soil organisms, crops, or livestock.

There is no evidence of any effect from Red Radish Extract on soil organisms, crops, or livestock from the production of Red Radish Extract.

10. Safety information about the substance including a Material Safety Data Sheet (MSDS) and a substance report from the National Institute of Environmental Health Studies

No Material Safety Data Sheet for Red Radish Extract was not found. No substance report for Red Radish Extract from the National Institute of Environmental Health Studies was found.

11. Research information about the substance which includes comprehensive substance research reviews and research bibliographies, including reviews and bibliographies which present contrasting positions to those presented by the petitioner in supporting the substance's inclusion on or removal from the National List. For petitions to include non-organic agricultural substances onto the National List, this information item should be responded to with research concerning the availability of organic alternatives.

Safety Reviews*:*

JECFA (1982). Toxicological evaluation of certain food additives. WHO Food Additives Series No. 17. Twenty-sixth meeting of the Joint WHO/FAO Expert Committee on Food Additives.

References:

Becci P.J., Hess F.G., Gallo M.A., Johnson W.D. and Babish J.G. (1983a) Subchronic feeding study of grape colour extract in beagle dogs. *Food Chemical Toxicology* **21**, 75-77.

Becci P.J., Hess F.G., Babish J.G., Gallo M.A. and Voss K.A. (1983b) Reproduction study of grape colour extract in rats. *Food Chemical Toxicology* **21**, 79-83.

Brown J.P. & Dietrich P.S. (1979) Mutagenicity of plant flavonols in the *salmonella*/mammalian microsome test. *Mutation Research* **66**, 223-240.

Cox G.E. and Babish J.G. (1978) Evaluation of the safety of dietary administration of special grape color powder (Type BW-AT) on reproduction, lactation, and maturation when fed to Sprague-Dawley rats. Food and Drug Research Laboratories. Lab. No. 5417.

Ferguson L.R., van Zijl P., Holloway W.D. and Jones W.T. (1985) Condensed tannins induce micronuclei in cultured V79 Chinese hamster cells. *Mutation Research* **158**, 89-95.

Haveland-Smith R.B. (1981) Evaluation of the genotoxicity of some natural food colours using bacterial assays. *Mutation Research* **91**, 285-290.

Horwitt M.K. (1933) Observations on behavior of the anthocyan pigment from concord grapes in the animal body. *Proceeding of the Society for Experimental Biology and Medicine* **30**, 949-951.

MacGregor J.T. & Jurd L. (1978) Mutagenicity of plant flavonoids: Structural requirements for mutagenic activity in *Salmonella typhimurium*.. *Mutation Research* **54**, 297-309.

Marmion, D.M.; Handbook of U.S. Colorants for Foods, Drugs, Cosmetics and Medical Devices. 3rd Ed.; John Wiley & Sons, Inc.: New York, New York, 1991.

Pourrat H., Bastide P., Dorier P., Pourrat M.A. and Tronche P. (1967) Pr_paration et activit_ th_rapeutique de quelques glycosides d'anthocyanes. *Chimie Th_rapeutique* **2**, 33-38.

Stevens K.R. and Gallo M.A. (1977) Thirty-day dose range finding study of Welch's grape extract in rats. Food and Drug Research Laboratories. Lab No. 5388.

Viola M. & Nosotti A. (1978) Applicazion del test di Ames su Alcuni coloranti. *Bollettino Chimico Farmaceutico* **117**, 402-415.

See Attachment #3 for information concerning the history and culinary uses of red radishes.

Commercial Availability Research:

As justification for this petition to place Red Radish Extract for use as a food coloring substance on National List section §205.606, we have done considerable research into the commercial availability of organic forms of Red Radish Extract.

CBI Deleted—commercial availability information

CBI

CBI Deleted

CBI Deleted—commercial availability information

CBI

12. Petition Justification Statement which provides justification for any of the following actions requested in the petition:

Natural colors have historically been an essential component of many food products. Practically all consumers judge the palatability of foods not only on flavor, texture, and aroma, but also on appearance. A large number of these consumers would find foods that did not meet their expectations for vibrant yet reliable colors to be unappealing and perhaps would suspect that they are not sufficiently nutritious or even, in some cases, safe to eat. Consumer acceptance of these foods is therefore based in large part upon the ability of processed food manufacturers to utilize food colors to maintain expected and desirable appearances for their products.

Organic consumers expect no less from their foods. Organic foods are chosen by consumers because they know that they are healthy and reliable, but also because they look good to consumers. For many foods, a large part of this positive appearance is due to the use of natural colors. Packaged organic black cherry yogurt looks like delicious yogurt with fresh black cherries swirled in because of the addition

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of grape juice. Organic portabello mushroom veggie hot dogs resemble a “traditional” hot dog due to the addition of paprika. Organic strawberry cheesecake looks like, well, strawberry cheesecake through the addition of beet juice. In all cases, the consumer is guaranteed that in addition to the great flavor and health benefits of eating organic foods, they also have the expected appearance and a highly desirable palatability.

The use of natural colors in organic and traditional foods is critical due to the processes involved in food production. In many processes there is at least one and occasionally several heating steps involved in the conversion of raw ingredients to final food products. In other cases the blending of ingredients changes the pH or increases the rate of oxidation. These have a deleterious effect on the colors in the raw materials, turning a bright red strawberry into something else entirely—something that consumers of traditional and organic foods might find unpalatable. Supplementing or replacing the naturally-contained color in the raw materials of food products with small amounts of natural colors ensures that the finished food products maintain the appeal of natural, unprocessed foods.

CBI Deleted—commercial availability information

CBI

organic handlers who incorporate natural colors into their food products. This petition, among others filed by us and others for natural colors, will work to fill this vacuum, and will provide organic handlers and the growing organic industry with a necessary continuity that is essential to eliminate the possibility of disruptions in production, the need for product reformulation, and the requirements for new product

labeling. While work towards a certified organic process for Red Radish Extract used as a coloring material continues, this petition and others will work to minimize the potential impact of the October 2007 sunset for “Colors, non-synthetic sources only” to the organic industry.

While IACM supported the renewal of “Colors, non-synthetic sources only” to the National List section 205.605(a), we do recognize that there were procedural difficulties with its initial placement on the National List that warranted its removal for legal reasons. The members of IACM have substantial interest in the potential growth of the organic industry, and we see the value in developing certified organic processes for our coloring materials. Should this petition be approved, Red Radish Extract used as a coloring material will be supplied to our organic customers by our member companies only until such a time as processes for certified organic Red Radish Extract that can be used as a coloring material are commercially available. Until that time, our customer organic handlers will be able to incorporate a spectrum of vibrant natural colors into their products, and the consumers will continue to purchase organic food products that meet their desires for a healthy, colorful diet.

13. Commercial Confidential Information Statement:

CBI Deleted—commercial availability information

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List of Attachments

Attachment #1: Technical Advisory Panel Review of “Colors, Non-Synthetic Sources Only”
Attachment #2: JECFA Evaluation of Anthocyanins
Attachment #3: Information concerning the history, medicinal value, and culinary uses of red radishes

OVERVIEW OF FOOD COLOR ADDITIVES

Prepared for the USDA National Organic Program and the National Organic Standards Board

October 14, 2005

This paper provides a general overview of color additives and how they are regulated in the United States. Use of colors in organic food production and potential adverse effects from the consumption of some specific colorants also are discussed.

I. EXECUTIVE SUMMARY

Colors are defined as any dye, pigment, or other substance that can impart color to a food, drug, or cosmetic or to the human body. Colors are regulated in the United States by the U.S. Food and Drug Administration (FDA) and are categorized either as "certifiable" (those derived primarily from petroleum and known as coal-tar dyes) or "exempt from certification" (those obtained largely from mineral, plant, or animal sources). Currently, there are no GRAS ("generally recognized as safe") exemptions for color additives. Consequently, all color additives are subject to premarket approval requirements. To obtain approval from FDA for a new color additive, the manufacturer must submit a petition demonstrating the safety and suitability of the new color additive or new use. FDA is then responsible for evaluating the petition and determining whether the color additive is safe for human consumption. Additionally, the decision regarding batch certification is made during FDA's review of the petition. If required, a sample from each manufactured batch must be submitted to FDA for analysis and certification. With this regulatory process, color additives generally have a good safety record; however, some adverse reactions have been noted. Specifically, allergic effects to Yellow No. 5 and carmine and cochineal extract have been observed. Additionally, possible carcinogenic effects have led FDA to ban uses of FD&C Red No. 3 and FD&C Red No. 2.

II. CHARACTERIZATION

Color additives are defined as any dye, pigment, or other substance that can impart color to a food, drug, or cosmetic or to the human body. Color additives include those that are white, black, and gray (Barrows et al., 2003). They also may include any chemical that reacts with another substance and causes formation of a color. In the United States, FDA is responsible for regulating color additives. For regulation purposes, FDA categorizes colors as "certifiable" (those derived primarily from petroleum and known as coal-tar dyes) and "exempt from certification" (those obtained largely from mineral, plant, or animal sources).

Certifiable colors can be further categorized into straight colors, mixtures, and dyes and lakes. Straight colors are those color additives that have not been mixed or chemically reacted with any other substance. Mixtures are the resulting color additives that are formed by mixing one color additive with one or more color additives or non-colored diluents, without a chemical reaction. Dyes are defined as those that "...dissolve in water

and are manufactured as powders, granules, liquids or other special purpose forms. They can be used in beverages, dry mixes, baked goods, confections, dairy products, pet foods and a variety of other products" (FDA, 1993). Lakes are the water insoluble form of the dye. Lakes tend to be more stable than dyes and ideal for coloring products containing fats and oils or items lacking sufficient moisture to dissolve dyes. Some examples where lakes are used include coated tablets, cake and donut mixes, hard candies, and chewing gums. Additionally, certifiable colors that are added to food are chemically classified as azo, xanthene, triphenylmethane, and indigoid dyes.

III. REGULATION

A. History

Color additives were initially regulated in the United States under the U.S. Department of Agriculture's (USDA) Bureau of Chemistry. In 1906, the Food and Drugs Act was passed by Congress, which prohibited the use of poisonous or deleterious colors in confectionery and the coloring or staining of food to conceal damage or inferiority. In 1927, responsibility of the Food and Drugs Act was transferred to FDA. Increasing government oversight, the Federal Food, Drug, and Cosmetic Act (FFDCA) was passed in 1938 and established the three following categories for colors:

- **FD&C:** colors used in foods, drugs and cosmetics;
- **D&C:** colors used in drugs and cosmetics when in contact with mucous membranes or ingested; and
- **Ext. D&C:** colors used in products applied externally.

The FFDCA mandated a listing of those coal-tar colors that were determined to be "harmless and suitable" for use in foods, drugs, and cosmetics. FDA interpreted "harmless" to mean harmless at any level (Francis, 2000). Additionally, the FFDCA required the listing of new colors, mandated the previously voluntary certification program for batches of listed color with associated fees, and contained adulteration and misbranding provision for the use of coal-tar colors in food, drugs, and cosmetics (Barrows et al., 2003).

The Color Additive Amendments to the FFDCA were established in 1960 because FDA's interpretation of "harmless" was not workable. Under the Color Additive Amendments, "color additives" were defined and a requirement was established that only color additives (except coal-tar hair dyes) listed as "suitable and safe" for a given use could be used in foods, drugs, cosmetics, and medical devices. A current listing of FDA approved colorants, including those that do and do not require certification, is provided in Table 1 (Barrows et al., 2003). As illustrated in Table 1, all of these colorants are straight colors.

1 **Table 1. FDA Approved Food Color Additives**

2

21 CFR Section	Straight Color	Use and Restrictions
Color Additives Subject To Certification		
74.101	FD&C Blue No. 1	Foods generally
74.102	FD&C Blue No. 2	Foods generally
74.203	FD&C Green No. 3	Foods generally
74.250	Orange B	Casings or surfaces of frankfurters and sausages, NTE 150 ppm
74.302	Citrus Red No. 2	Skins of oranges not intended or used for processing, NTE 2.0 ppm (by weight)
74.303	FD&C Red No. 3	Foods generally
74.340	FD&C Red No. 40	Foods generally
74.705	FD&C Yellow No. 5	Foods generally
74.706	FD&C Yellow No. 6	Foods generally
Color Additives Exempt From Certification		
73.30	Annatto extract	Foods generally
73.35	Astaxanthin	Salmonid fish feed
73.40	Dehydrated beets (beet powder)	Foods generally
73.50	Ultramarine blue	Salt for animal feed
73.75	Canthaxanthin	Foods generally, NTE 30 mg/lb of solid or semisolid food or per pint of liquid food; broiler chicken feed; salmonid fish feed
73.85	Caramel	Foods generally
73.90	ß-Apo-8'-carotenal	Foods generally, NTE 15 mg/lb solid, 15 mg/pt liquid
73.95	ß-Carotene	Foods generally
73.100	Conchineal extract; carmine	Foods generally
73.125	Sodium copper chlorophyllin	Citrus-based dry beverage mixes, NET 0.2% dry mix
73.140	Toasted partially defatted cook cottonseed flour	Foods generally
73.160	Ferrous gluconate	Ripe olives
73.165	Ferrous lactate	Ripe olives
73.169	Grape color extract	Nonbeverage food
73.170	Grape skin extract (enocianina)	Still and carbonated drinks and ades; beverage bases; alcoholic beverages
73.185	Haematococcus algae meal	Salmonid fish feed
73.200	Synthetic iron oxide	Sausage casings, NTE 0.1%

21 CFR Section	Straight Color	Use and Restrictions
		(by weight); dog and cat food, NTE 0.25% (by weight)
73.250	Fruit juice	Foods generally
73.260	Vegetable juice	Foods generally
73.275	Dried algae meal	Chicken feed
73.295	Tagetes (Aztec marigold mean and extract)	Chicken feed
73.300	Carrot oil	Foods generally
73.315	Corn endosperm oil	Chicken feed
73.340	Paprika	Foods generally
73.345	Paprika oleoresin	Foods generally
73.355	Phaffia yeast	Salmonid fish feed
73.450	Riboflavin	Foods generally
73.500	Saffron	Foods generally
73.575	Titanium dioxide	Foods generally, NTE 1% (by weight)
73.600	Turmeric	Foods generally
73.615	Turmeric oleoresin	Foods generally

The Color Additive Amendments also established the "Delaney Clause" that prohibited the listing of a color additive shown to be carcinogenic.

B. Petition Process

Under the current regulatory system, FDA is responsible for ensuring the safety of new food additives, including colors. However, food additive petitions are not required for food additives that are identified as "generally recognized as safe" (GRAS) substances. Currently, there are no GRAS ("generally recognized as safe") exemptions for color additives. Consequently, all color additives are subject to premarket approval requirements. These requirements are listed in Title 21 of the Code of Federal Regulations (CFR), Part 71. In filing a color additive petition, the manufacturer is responsible for providing FDA with information including, but not limited to the following:

- Identification of the food additive;
- Physical, chemical, and biological properties;
- Chemical specifications;
- Manufacturing process description;
- Stability data;
- Intended uses and restrictions;
- Labeling[1];

[1] Any labeling that will be required by applicable provisions of the FFDCA on the finished food by reason of the use of the food additive.

- Tolerances and limitations[2];
- Analytical methods for enforcing chemical specifications;
- Safety studies; and
- Estimate of probable exposure.

C. Safety Assessment

A color additive petition must demonstrate the safety and suitability of the new color additive or new use. FDA is responsible for evaluating petitions and determining whether the additive is safe for human consumption. Generally, this determination is made by examining the following parameters:

- History of use or natural occurrence;
- Consumption ratio, if applicable;
- Exposure levels;
- Inherent toxicity of the substance;
- Toxicological data on the substance or on structurally-related compounds; and
- Metabolism of the substance (either know of forecasted on the basis of data for structurally-related compounds).

FDA's safety assessment includes a review toxicity data such as the results of controlled animal studies. Ideally, a complete range of data, including short- and long-term toxicity studies, as well as studies that examine possible reproductive, carcinogenic, mutagenic, and sensitization characteristics of the color additive would be available for review. Sometimes a complete set of toxicology data is not available. One method of gaining additional insight on a color lacking a complete set of data is to evaluate the toxicity of structurally related substances. By evaluating structurally related substances, scientists can try to determine how the compound is absorbed, distributed, and metabolized within the body, and how it may act on target organs in the body. Based on these data and various safety factors, FDA determines a safe exposure level for the color additive.

FDA then compares the safe exposure level to the amount likely to be consumed in food taking into consideration the composition and properties of the substance and the proposed conditions of use. Because the absolute safety of any substance can never be proven, FDA must determine if the additive is safe under the proposed conditions of use, based on the best scientific knowledge available. For more information, see http://vm.cfsan.fda.gov/~dms/opa-cg8e.html.

[2] According to 21 CFR Part 571, "If the food additive is one for which a tolerance limitation is required to assure its safety, the level of use proposed should be no higher than the amount reasonably required to accomplish the intended physical or other technical effect, even though the safety data may support a higher tolerance."

D. Batch Certification

As described in Section II, FDA requires certification of every manufactured batch of some color additives. Color additives requiring and exempt from batch certification are listed in Table 1.

Batch certification is required when the composition of the color needs to be controlled in order to protect public health. Procedures for color additive batch certification are available in 21 CFR Part 80. Under these procedures, a sample from each manufactured batch of certifiable color additive, as well as a "Request for Certification," must be submitted to FDA's Color Certification Branch. The "Request for Certification" should provide information regarding the batch weight, storage conditions, and the use for which it is being certified. FDA is then responsible for evaluating the batch's physical appearance and performing chemical analyses including, but not limited to the following:

- Purity (total color content);
- Moisture;
- Residual salts;
- Unreacted intermediates;
- Colored impurities other than the main color;
- Any other specified impurities; and
- Heavy metals (lead, arsenic, and mercury).

If the sample meets FDA's requirements, FDA will issue a certificate for the batch that identifies the color additive, batch weight, uses for which the color additive is certified, the name and address of the owner, as well as other information. The batch also is assigned a unique lot number.

Colors that are exempt from certification are usually derived from plant or mineral sources and must comply with the identity and purity specification and use limitation described in their listing regulations. According to 21 CFR 71.1(c)G, "If exemption from batch certification is requested, the reasons why it is believed such certification is not necessary (including supporting data to establish the safety of the intended use)." Consequently, a petition for exemption from certification must show why such certification is not necessary for the protection of public health (21 CFR 71.18). Color additives that are exempt from batch certification for one use may be subject to batch certification for other uses. Because natural colorants are exempt from a lengthy certification process, there has been a strong trend over the past 50 years toward the use of these color additives as compared to synthetic coal-tar dyes (Francis, 2000).

IV. ADVERSE EFFECTS

Although food colors generally have a good safety record, some adverse reactions have been noted. For example, Yellow No. 5 (listed as tartrazine on medicine labels; a color found widely in beverages, desserts, processed vegetables, drugs, makeup, and many other products) causes itching or hives in a small population sub-group (FDA, 2001).

Another color that causes allergic reactions is carmine and cochineal extract. Carmine and cochineal extract are scarlet red pigments that come from the female coccid insect *Dactylopius coccus* var. Costa (family Dactylopiidae, superfamily Coccoidea), which is parasitic on several species of cacti, particularly the cochineal figs produced by prickly pear (Opuntia) cactus *Nopalea cochenillifera*. There have been several case reports of anaphylaxis and urticaria resulting from ingestion of food or drink containing carmine (Beaudouin et al., 1995; Baldwin et al., 1997; DiCello et al., 199a,b; Chung et al., 2001).

In 1960, FDA banned uses of FD&C Red No. 3 including cosmetics and externally applied drugs because large amounts of the color caused thyroid tumors in male rats (FDA, 2001). In 1976, FDA issued a ban on FD&C Red No. 2 because there appeared to be a statistically significant increase in malignant tumors when fed high doses of the color (FDA, 2001).

V. USE OF COLORS IN ORGANIC FOODS

Colors are currently on the National List of Allowed and Prohibited Substances for use in organic foods. Colors were not added to the National List as the result of a petition. Instead, they were included among substances initially placed on the National List when USDA promulgated regulations pursuant to the Organic Food Production Act of 1990. According to 21 CFR Part 205.605, nonagricultural (nonorganic) colors are allowed as ingredients in or on processed food products labeled as "organic" or "made with organic." Only nonsynthetic colors (as a group) are allowed.

References:

Baldwin J.L., Chou A.H., and Solomon W.R. 1997. Popsicle-induced anaphylaxis due to carmine dye allergy. Annals of Allergy, Asthma & Immunology 79:415-419.

Barrows J.N., Lipman A.L., Bailey C.J. 2003. Color Additives: FDA's Regulatory Process and Historical Perspectives. Available at: http://www.cfsan.fda.gov/~dms/col-regu.html.

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Chung K., Baker J.R., Baldwin J.L., and Chou A. 2001. Identification of carmine allergens among three carmine allergy patients. Allergy 56(1):73-77.

DiCello M.C., Baldwin J.L., Myc A., and Baker J.R. 1999a. Anaphylaxis after ingestion of yogurt colored with carmine. Annals of Allergy, Asthma, & Immunology 82:73 (Abstract).

DiCello M.C., Myc A., Baker J.R., and Baldwin J.L. 1999b. Anaphylaxis after ingestion of carmine colored foods: two case reports and a review of the literature. Allergy and Asthma Proceedings 20:377-382.

FDA. 2001. Food Additives Fact Sheet. Available at: http://www.cfsan.fda.gov/~dms/cos-221.html.

FDA. 1993. Food, Nutrition, and Cosmetics Questions & Answers. Available at: http://www.cfsan.fda.gov/~dms/qa-topad.html.

Francis F.J. (2000) Safety assessment of flavor ingredients. In: Watson D.H. (ed.). Food Chemical Safety. Volume 2. Woodhead Publishing Limited: Cambridge, England. Pp. 173-206.

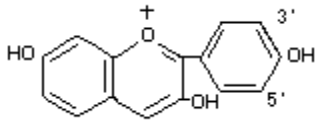
ANTHOCYANINS

Explanation

These compounds have not previously been reviewed by the Joint FAO/WHO Expert Committee on Food Additives.

Introduction

Anthocyanins represent a large group of water-soluble plant pigments of the 2-phenylbenzophyrylium (flavylium) structure (Kuhnau, 1976). The class, "Anthocyanins", consists of some 200 or more compounds (Parkinson & Brown, 1981) chemically combined to a sugar moiety (glucose < rhamnose < galactose < xylose < arabinose) of which the most common are:



Anthocyanin structure

Compound	Carbon ring B substitution 3'	5'
pelargonidin	-H	-H
cyanidin	-OH	-H
delphinidin	-OH	-OH
peonidin	$-OCH_3$	-H
petunidin	$-OCH_3$	-OH
malvidin	$-OCH_3$	$-OCH_3$

The blue to red colour imparted by the anthocyanins depends largely upon the pH of the medium (Francis, 1977). The anthocyanins normally exist as glycosides; the aglycone component alone is extremely unstable.

The anthocyanin pigments present in grape-skin extract consist of diglucosides, monoglucosides, acylated monoglucosides, and acylated diglucosides of peonidin, malvidin, cyanidin, petunidin and delphinidin. The amount of each compound varies depending upon the variety of grape and climatic conditions.

BIOLOGICAL DATA

BIOCHEMICAL ASPECTS

Absorption, distribution and excretion

Anthocyanins are poorly absorbed from the gastrointestinal tract. Anthocyanins (notably delphinidin) extracted from concord grapes were administered to rats by either gavage (100 mg) or by percutaneous injection (50 mg) and the urine tested for unchanged anthocyanins by an HCl-acid red test (Horwitt, 1933). Anthocyanin was detected in the urine of rats administered anthocyanin by the percutaneous route but not by gavage. In studies in dogs (Horwitt, 1933) administered anthocyanin (500 mg) by gastric fistula, no

urinary coloration was demonstrated. However, in the rabbit, 1-2% of an oral dose of anthocyanin (500 mg) was present in the urine as the unchanged pigment. It should be noted that the HCl-acid red test used in this study would only detect unchanged anthocyanins (Scheline, 1978). If the anthocyanins were transformed into colourless pseudobases or pale anhydrolases prior to absorption and excretion, they would not be detected (Kuhnau, 1976).

The absence of pigmented urine in normal individuals ingesting anthocyanin-containing foods in humans coupled with the apparent lack of metabolism of anthocyanins has been interpreted as showing that gastrointestinal absorption of these compounds does not occur (Clark & Mackay, 1950). Clinical studies have reported anthocyaninuria in patients with a beet allergy, following the ingestion of large amounts of beets (Zindler & Colovos, 1950). However, this has been identified as betaninuria, and is related to the excretion of betanin, rather than anthocyanins (Forrai et al, 1968).

Tissue disposition of anthocyanosides derived from Vaccinium myrtillus (approximately 25% anthocyanins) was examined in Charles River rats following intraperitoneal (i.p.) or intravenous (i.v.) injection. Following acute administration by either route, anthocyanins were found to distribute rapidly into the tissues.

Accumulation was primarily in the kidney, skin, liver, heart and lung (Lietti & Forni, 1976). There was also some indication of lymph node uptake of the anthocyanins. Elimination of the compound occurred primarily via the kidney (25-29%/24 hours) and bile (15-18%/24 hours). Because of the high urinary excretion rate in these studies, the anthocyanins are considered to be eliminated by both glomerular filtration and renal tubular excretion (Lietti & Forni, 1976).

Metabolism

Studies in rats have shown that some anthocyanins (notably pelargonidin, delphinidin, malvidin) were subject to degradation by intestinal bacteria (Griffiths & Smith, 1972a, b). p-hydroxyphenyl-lactic acid was detected in the urine of rats following the oral administration of pelargonidin (a 3',3-diglycoside of pelargonidin). Decoloration of "anthocyanin" by rat caecal cell extracts has been reported (Haveland-Smith, 1981). Anthocyanin extracts incubated with human faecal suspensions for 2-3 days remained unchanged (as measured by a reduction in suspension colour).

The presence of 2 unidentified metabolites in the urine of rats after gavage with 100 mg of delphinidin has also been reported (Scheline, 1978). Rats gavaged with malvidin (a 3',5'-diglycoside of malvidin) had 3 unidentified metabolites present in the urine. These studies suggest that some of the metabolites of anthocyanins (aglycones) can be absorbed. Metabolism of anthocyanins may occur to a limited degree by ring fission and/or glycoside hydrolysis of the anthocyanins (Parkinson & Brown, 1981). Cyanidin, the most widespread anthocyanin, has not been shown to be attacked by intestinal bacteria (Scheline, 1968; Griffiths & Smith, 1972a).

Effects on enzymes and other biochemical parameters

Both pelargonidin and delphinidin have been shown to inhibit aldoreductase in the lens of rats (Varma & Kinoshita, 1976). In other studies, anthocyanin-3-monoglycosides (namely petunidin-, delphinidin- and malvidin-) extracted from grapes were found to increase the activity of alpha glucan phosphorylase and glutamic acid dicarboxylase but inhibit glycerol dehydrogenase, malate dehydrogenase and hexokinase (Carpenter et al., 1967).

Other studies have shown that anthocyanins are capable of chelating ions such as copper (Somaatmadja et al., 1964) and iodide (Moudgal et al., 1958). The iodide ion was observed in vitro to form a stable complex with the anthocyanins (Moudgal et al., 1958).

TOXICOLOGICAL STUDIES

Special studies on mutagenicity

Cyanidin chloride was not mutagenic when examined in the Ames assay using Salmonella typhimurium strain TA-98 with and without metabolic activation (arochlor 1254 induced rat liver S-9 fraction) (MacGregor & Jurd, 1978). Structure-activity testing of a large group of flavonols for mutagenic response in this assay system indicated that compounds of flavylium class were inactive.

Cyanidin and delphinidin were inactive in the Ames assay system using 5 different strains of Salmonella typhimurium (TA-1535, TA-100, TA-1537, TA-1538 and TA-98) with and without activation (Brown & Dietrich, 1979).

Anthocyanin was tested in both the Ames test using Salmonella typhimurium TA-1538 for mutagenicity and in another in vitro test employing E. coli Wf2 for induction of DNA damage. In both assay procedures with or without metabolic activation (using either rat caecal extracts or rat liver microsomes) anthocyanins were not found to induce any response (Haveland-Smith, 1981). Negative findings were also reported for the anthocyanins in a gene conversion assay using S. cerevisiae D4 (Haveland-Smith, 1981).

Special studies on pharmacology

In rabbits administered anthocyanin glycosides 6 g/kg (oral) or 500 mg/kg (i.p.) acutely, no adverse effect was noted on blood pressure. However, 100-200 mg/kg i.v. was shown to elicit a transcent hypotension accompanied by a decrease in respiratory amplitude. At 25 mg/kg i.v., diuretic effects were also reported. Anthocyanin also caused a vasodilation in the isolated rabbit heart (Pourrat et al., 1967).

In mice, anthocyanins given in oral doses of 500 mg/kg produced a sedative effect on the animals (Pourrat et al., 1967).

Improvements in visual acuity and darkness adaptation have been reported in humans for a short period of time, after receiving oral doses of up to 700 mg of the anthocyanins (Pourrat et al., 1967).

Special studies on reproduction

A 2-generation reproduction study was performed in rats (Sprague-Dawley) ingesting a grape-skin extract preparation that was prepared by spray drying the liquid form of the extract after addition of a carrier material (malto-dextrose). The preparation

contained approximately 3% anthocyanins. The test group received dietary levels of 7.5% or 15% of the grape-skin extract throughout the study. There were two concurrent control groups, one receiving the basal diet, the other receiving a diet containing 9% of the malto-dextrin used as a carrier to the grape-skin extract preparation. The F_{2a} generation (10/litter culled at 4 days) were maintained for 21 days post-partum, then autopsied. No differences in reproduction performance or indices including pup viability were apparent between control and dosed groups. At the high-dose level, both the F_{1a} and F_{2a} rats exhibited lower body weights than the concurrent controls. Body weights of the F_2 pups in the 7.5% group were marginally depressed. However, it should be noted that the

decrease in body weights was accompanied by a concomitant decrease in food intake. At week 6 and at termination of the studies, haematological and blood serum chemistry and urinalyses were carried out in the F_{1a} group. There were no compound-related effects. At week 18 of the study, rats in the F_{1a} group were sacrificed and absolute and relative organ weights determined, and a complete histological study was carried out in the principal organs and tissues. Decrease in organ weights of the liver, adrenal and thyroid occurred in the 15% group. There were no compound-related histological effects (Cox & Babish, 1978a).

Special studies on teratogenicity

The anthocyanin glycosides (an extract from currants, blueberries and elderberries) were reported not to be teratogenic in rats, mice or rabbits when given at dose levels of 1.5, 3 or 9 g/kg over 3 successive generations (Pourrat et al., 1967).

Acute toxicity

Animal	Route	LD_{50} (mg/kg bw)	Reference
Mice	i.p.	4 110	Pourrat et al., 1967
	i.v.	840	Pourrat et al., 1967
	Oral	25 000	Pourrat et al., 1967
Rats	i.p.	2 850	Pourrat et al., 1967
	i.v.	240	Pourrat et al., 1967
	Oral	20 000	Pourrat et al., 1967

Test animals were administered the anthocyanins (cyanidin, petunidin and delphinidin mixture extracted from currants, blueberries and elderberries) in doses from 0 to 25 000 mg/kg bw for mice and from 0 to 20 000 mg/kg for rats. Following i.v. or i.p. administration, toxic doses of anthocyanins produced sedation, convulsions and finally death.

Short-term studies

Weanling male and female Wistar rats (20/group) were fed a diet containing anthocyanin extract at levels equivalent to 3000 mg/day or 6000 mg/day for a period of 90 days. A group of concurrent controls were also used in the study. The doses of anthocyanin administered were estimated to be 5 and 10 times, respectively, the level that a human would ingest. No differences were observed between the test animals and controls in survival, growth or histopathology of the principal tissues at the termination of the study (Pourrat et al., 1967).

In another study, guinea-pigs received 3000 mg/kg of anthocyanin in the diet for 15 days. No adverse effects were reported (Pourrat et al., 1967).

Male and female beagle dogs (4/sex/dose) received either 0, 7.5% or 15% of grape-skin extract (approximately 2.39% anthocyanin by weight) in the diet for 90 days. No differences were noted between control and treated animals in body weights, growth, survival, clinical chemistries (haematology, biochemistry or urinalysis), organ weights or pathological lesions (gross or microscopic) (Cox & Babish, 1978a).

OBSERVATIONS IN MAN

Man is naturally exposed to anthocyanins through the ingestion

of fruits and vegetables. Levels of exposure under normal dietary conditions have not been established.

Information on the metabolism and toxicity of the anthocyanins is limited. Its interpretation is complicated because the anthocyanins represent a large group of chemically-related substances and the effect observed with one defined anthocyanin may not be applicable to another. The available information suggests that anthocyanins are poorly absorbed from the gastrointestinal tract. Metabolism is limited and may be due to the activity of the intestinal bacterial flora. The metabolites of anthocyanins have not been identified. However, the insensitivity of the assay techniques used for measuring unmetabolized anthocyanins may result in a significant underestimate of the degree of absorption and metabolism of the anthocyanins (Kuhnau, 1976).

Comments

Toxicological studies are limited, and have been carried out with mixtures extracted from a variety of fruits. The available data indicate that such extracts are of a very low order of toxicity. Diets containing 7.5% or 15% of a grape-skin extract preparation (approximately 3% anthocyanin) had no effect on the reproductive performance of rats in a 2-generation reproductive study. The lower body weights of offspring were related to a concomitant decrease in food intake. At the highest level tested, there was a decreased organ weight of the liver, adrenal and thyroid. There were no compound-related histological effects. No compound-related effects were observed in a short-term study in which dogs were fed diets containing 7.5% or 15% of the grape-skin extract preparation.

EVALUATION

Level causing no toxicological effect (Grape-skin extract preparation)

Rat (young): 7.5% of the diet equivalent to 7500 mg/kg bw.

Estimate of acceptable daily intake for man

0-2.5 mg/kg bw.*

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* Anthocyanins (present in the grape-skin preparation at level of approximately 3%).

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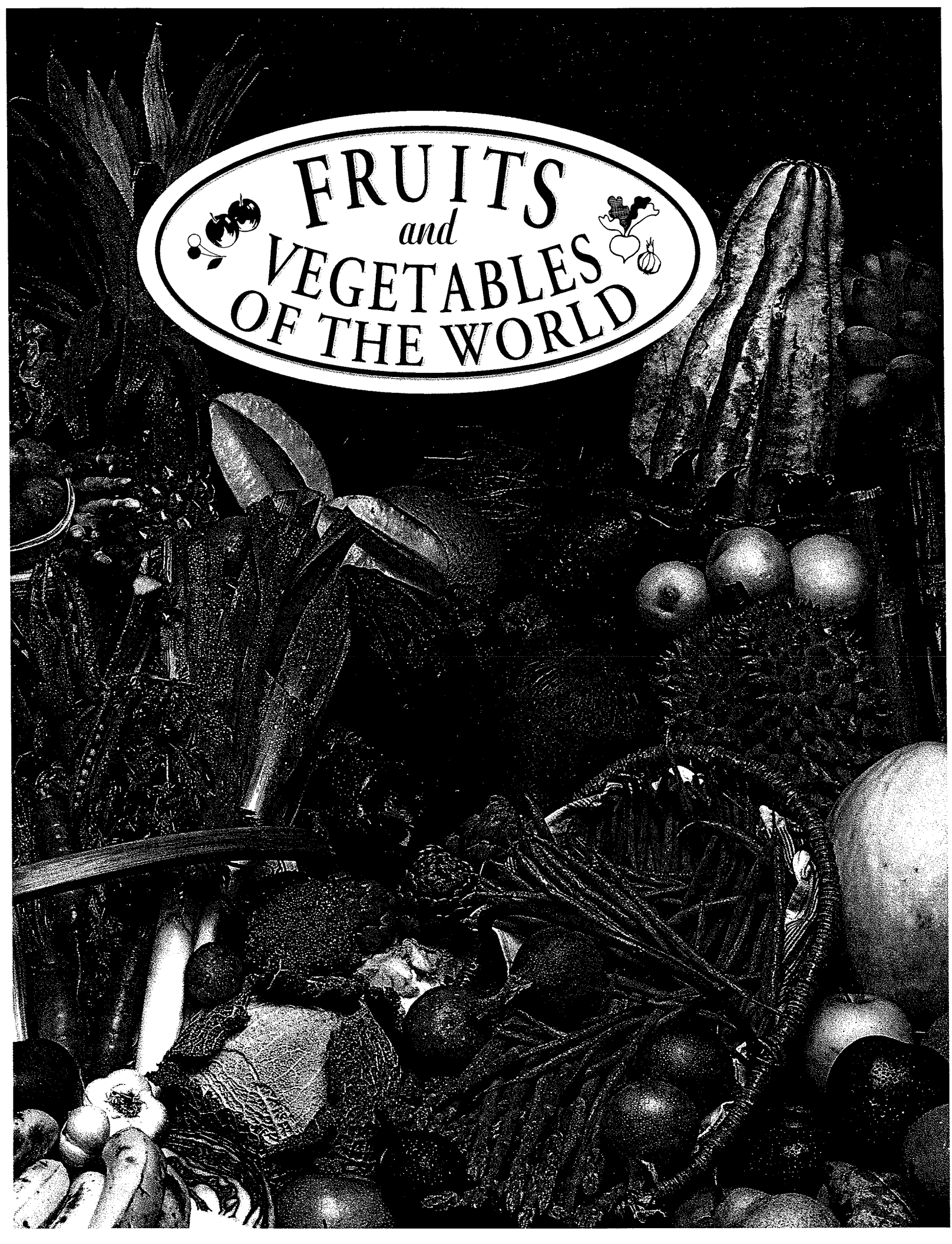
See Also:
Toxicological Abbreviations
ANTHOCYANINS (JECFA Evaluation)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VEGETABLES
OF THE WORLD

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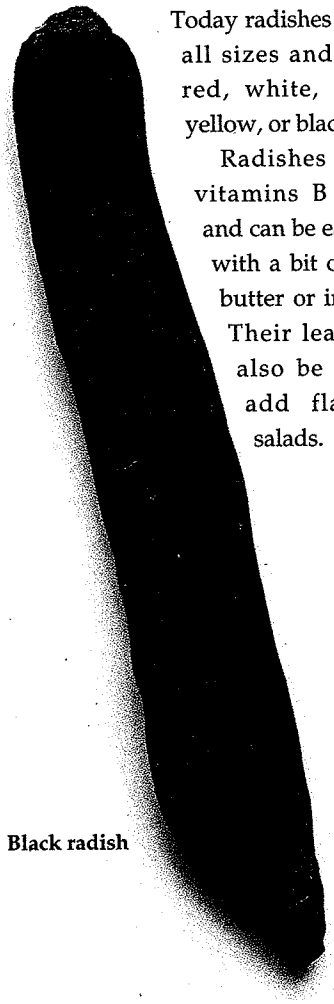
additional supplies during high-consumption periods like winter. It is sold with part of its stem and leaves. Once celeriac is scraped and the leaves removed, it can be eaten raw in salads.

White radish

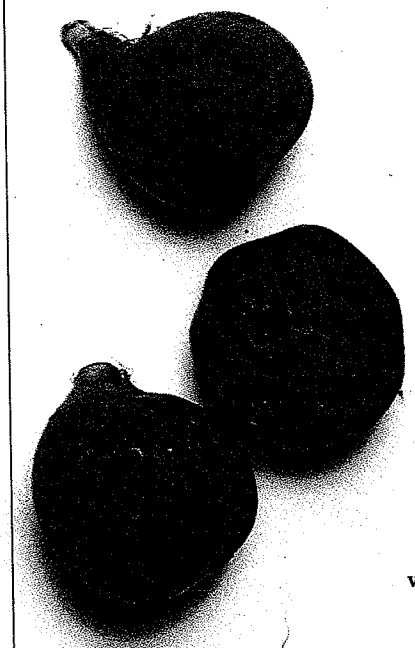
Radish. The word radish comes from the Latin *radix*, which means root. The protruding section we eat is in fact a hypocotyl, namely the end of the stem that is prolonged by the real root. The radish is a very ancient vegetable. Hieroglyphics from Karnak provide evidence that radishes were eaten by the pyramid builders. In Ancient Egypt, and later in Greece and Rome, only the large black radishes existed. It was not until the sixteenth century that the small red radishes appeared. Today radishes come in all sizes and colors: red, white, orange, yellow, or black.

Radishes contain vitamins B and C, and can be eaten raw with a bit of salt or butter or in salads. Their leaves can also be used to add flavor to salads.

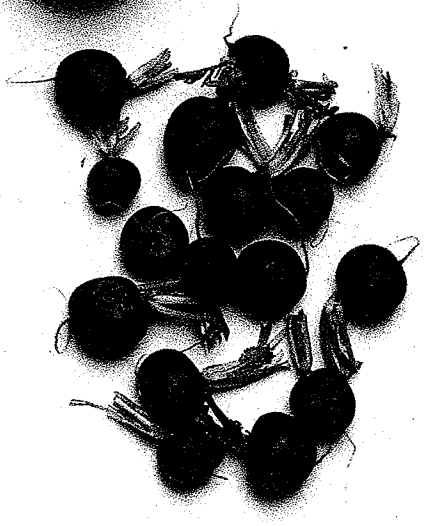


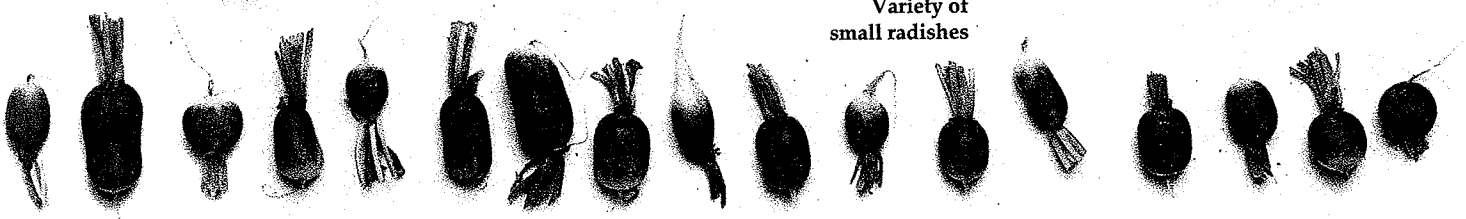
Black radish

Small and discreet, the red radish may seem to be a perfectly innocuous vegetable, but appearances can be deceptive! In northern countries it is still thought to possess magical properties. The juice and leaves of the radish are also said to heighten sexual desire.



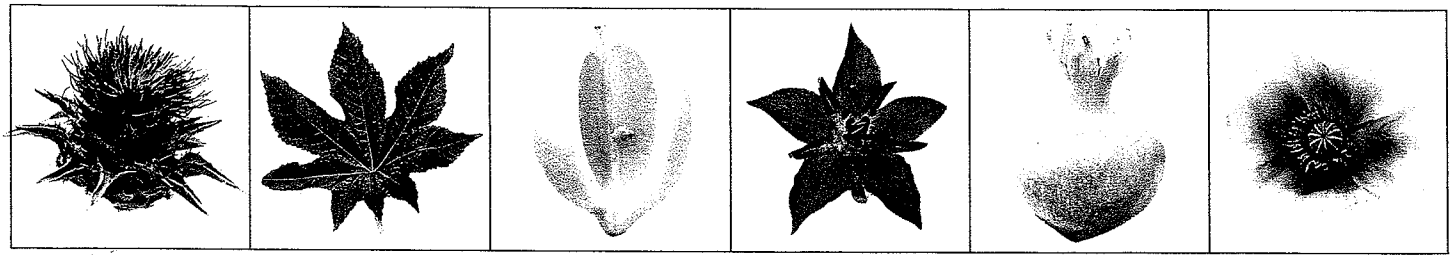
Other radish varieties





Variety of small radishes

ANDREW CHEVALLIER



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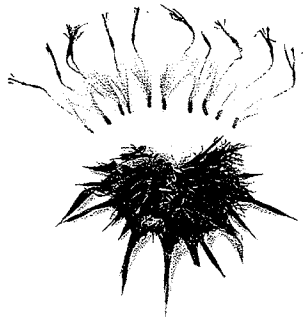

"First the word, then the plant, lastly the knife."
Aesculapius of Thassaly *c.* 1200 BC

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IMPORTANT NOTICE

Do not try self-diagnosis or attempt self-treatment for serious or long-term problems without first consulting a qualified medical herbalist or doctor. Do not take any herb without first checking the cautions in the relevant herb entry (see pp. 54–281) and the Essential Information on pp. 298–299. Do not exceed any dosages recommended. Always consult a professional if symptoms persist. If taking prescribed medicines, seek professional advice before using herbal remedies. Take care to identify plants correctly, and do not harvest restricted species.

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Quercus robur
(Fagaceae)
ENGLISH OAK

DESCRIPTION Slow-growing, long-lived, deciduous tree reaching 150 ft (45 m). Has deeply lobed leaves, long catkins, and green to brown fruit (acorns).

HABITAT & CULTIVATION English oak grows throughout Europe, in woods, forests, and along roadsides. The tree is also cultivated for its lumber, which is extremely durable. The bark is collected in spring and the fruit in autumn.


Oak bark

PARTS USED Bark, galls (growths produced by insects or fungi).

CONSTITUENTS English oak bark contains 15–20% tannins (including phlobatannin, ellagitannins, and gallic acid). Oak galls contain about 50% tannins.

HISTORY & FOLKLORE Sacred to the Druids, the oak tree has been esteemed in European herbal medicine for its astringent bark, leaves, and acorns. The bark has also been used to tan leather and to smoke fish. Oak lumber was formerly used to build the naval fleets of European nations, and whole forests were cleared in order to meet the shipbuilders' needs.

MEDICINAL ACTIONS & USES English oak bark, prepared as a decoction, is used as a gargle to treat sore throats and tonsillitis. It may also be applied as a wash, lotion, or ointment to treat hemorrhoids, anal fissures, small burns, and other skin problems. Less commonly, a decoction of the bark is taken in small doses to treat diarrhea, dysentery, and rectal bleeding. Powdered oak bark may be sniffed to treat nasal polyps, or sprinkled on eczema to dry the affected area. Oak galls are very astringent. They are used, in small quantities, in place of bark.

CAUTION Do not take common oak bark internally for more than 4 weeks at a time.

SELF-HELP USE Hemorrhoids, p. 302.

Quillaja saponaria
(Rosaceae)
SOAP BARK

DESCRIPTION Evergreen tree growing to 70 ft (20 m). Has glossy oval leaves, white flowers, and star-shaped fruit.

HABITAT & CULTIVATION Soap bark is native to Chile and Peru, and is now cultivated in California and India for medicinal and industrial use. The bark is gathered throughout the year.

PART USED Inner bark.

CONSTITUENTS Soap bark contains up to 10% triterpenoid saponins, calcium oxalate, and tannins. The saponins are strongly expectorant and can cause inflammation of the digestive tract.

HISTORY & FOLKLORE In Peru and Chile, soap bark has traditionally been used by Andean peoples as an alternative to soap for bathing and for washing clothes. The bark has been used medicinally by these peoples as an expectorant.

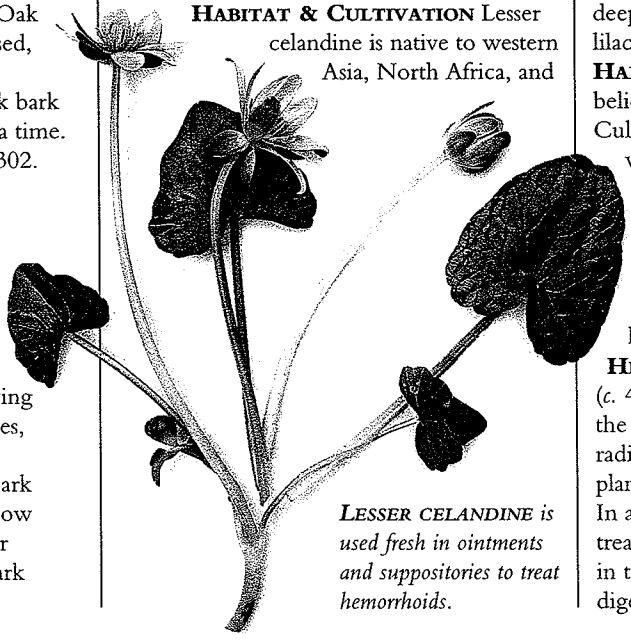
MEDICINAL ACTIONS & USES Soap bark has a long tradition of use as a treatment for chest problems. Its strong expectorant effect is beneficial in the treatment of bronchitis, especially in the early stages of the illness. Like other medicinal plants that contain saponins, soap bark stimulates the production of a more fluid mucus in the airways, facilitating the clearing of phlegm through coughing. Soap bark is useful for treating any condition featuring congested mucus within the chest, but it should not be used for dry, irritable coughs. Soap bark is also used externally, appearing in the formulations of dandruff shampoos.

CAUTIONS Use only under professional supervision. Given soap bark's irritant effect on the digestive tract, internal use must be carefully monitored.

Ranunculus ficaria
(Ranunculaceae)
LESSER CELANDINE, PILEWORT

DESCRIPTION Mat-forming perennial growing to 6 in (15 cm). Has small tubers, fleshy heart-shaped leaves, and shiny-petaled, brilliant yellow flowers.

HABITAT & CULTIVATION Lesser celandine is native to western Asia, North Africa, and Europe. Commonly found in woods, along roadsides, and in bare, open spaces, it is collected when it comes into flower in spring.


LESSER CELANDINE is used fresh in ointments and suppositories to treat hemorrhoids.

PARTS USED Aerial parts.

CONSTITUENTS Lesser celandine contains saponins, protoanemonin and anemonin, tannins, and vitamin C. Protoanemonin is antibacterial and irritant; it is absent from the dried herb.

HISTORY & FOLKLORE Lesser celandine has been used from the earliest times as a medicine for the relief of hemorrhoids and ulcers. The Greek physician Dioscorides, writing in the 1st century AD, noted that the plant blisters the skin, treats scabies and infected nails, and has a "watery virtue." In 1652, the herbalist Nicholas Culpeper recounted the medieval belief that simply carrying lesser celandine on one's person was sufficient to cure hemorrhoids.

MEDICINAL ACTIONS & USES Lesser celandine makes a useful ointment or suppository for treating hemorrhoids.

RELATED SPECIES Various other *Ranunculus* species have been used in herbal medicine, even though all are toxic and irritant to a greater or lesser degree. In North America, the Meskawi people used the flowers and stigma of the yellow water crowfoot (*R. delphinifolius*) as a snuff to provoke sneezing, and mixed it with other herbs to treat respiratory conditions such as mucus and nasal congestion.

CAUTION Do not take lesser celandine orally.

SELF-HELP USE Hemorrhoids, p. 302.

Raphanus sativus
(Cruciferae)
RADISH

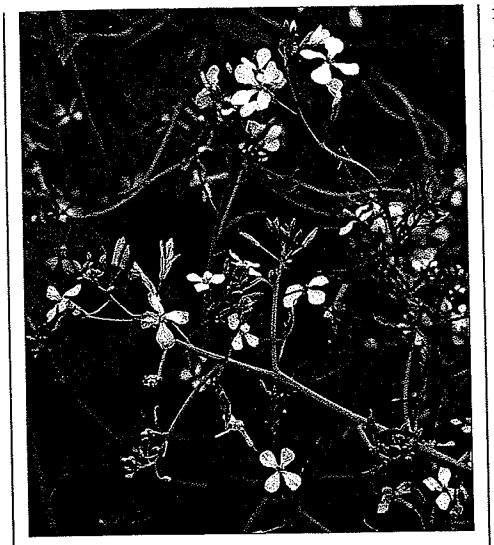
DESCRIPTION Bristly annual growing to about 3 ft (1 m). Has a swollen tap root, deeply cut compound leaves, pale violet to lilac flowers, and cylindrical seed pods.

HABITAT & CULTIVATION Radish is believed to be native to southern Asia. Cultivated varieties are grown around the world as vegetables and for medicinal use. The root is unearthed in autumn.

PART USED Root.

CONSTITUENTS Radish contains glucosilinates, which yield a volatile oil, raphanin, and vitamin C. Raphanin has antibiotic properties.

HISTORY & FOLKLORE Herodotus (*c.* 485–*c.* 425 BC) wrote that the builders of the pyramids in ancient Egypt were paid in radishes, onions, and garlic. In Egypt, the plant was used as a vegetable and a medicine. In ancient Rome, radish oil was applied to treat skin diseases. In China, radish was listed in the *Tang Materia Medica* (AD 659) as a digestive stimulant.



RADISH has been used since at least the 7th century to aid digestion.

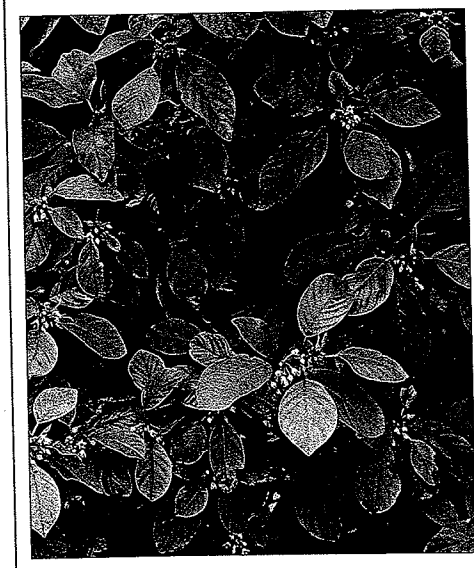
MEDICINAL ACTIONS & USES Radish stimulates the appetite and digestion. The common red radish is eaten as a salad vegetable and an appetizer. The juice of the black radish is drunk to counter gassy indigestion and constipation. Black radish juice has a tonic and laxative action on the intestines and indirectly stimulates the flow of bile. Consuming radish generally results in improved digestion, but some people are sensitive to its acridity and robust action. In China, radish is eaten to relieve abdominal distension. The root is also prepared "dry-fried" to treat chest problems.
CAUTIONS Some people may suffer indigestion after consuming radish or its juice. Radish should not be taken by people suffering from gastritis, peptic ulcer, or thyroid conditions, and it should not be taken for more than 3–4 weeks at a time.

Rauvolfia serpentina
(Apocynaceae)
INDIAN SNAKEROOT, SARPAGANDHA (HINDI)

DESCRIPTION Evergreen shrub growing to 3 ft (1 m). Has whorls of elliptical leaves, tiny pink and white tubular flowers, and glossy red berries.
HABITAT & CULTIVATION Indian snakeroot is native to much of southern and southeastern Asia, including India, Malaysia, and Indonesia. It is widely cultivated for medicinal use, notably in India and the Philippines. The root of plants at least 18 months old is unearthed in late winter.
PART USED Root.
CONSTITUENTS Indian snakeroot contains a complex mixture of indole alkaloids, including reserpine, rescinnamine, ajmaline, and yohimbine. Ajmaline has been used to regulate heartbeat.
HISTORY & FOLKLORE Indian snakeroot is listed in the *Charaka Samhita*, the earliest Ayurvedic medical text (*c.* 700 BC). The plant has been used since at least that time to treat mental illness and insomnia. Indian snakeroot's status as a healing plant was first recorded in Europe in 1785, but it was not until 1946 that conventional Western medicine recognized the herb's efficacy. After that date, the whole plant, and its reserpine extract in particular, were widely used in conventional medicine to lower high blood pressure and lessen the symptoms of mental illness.
MEDICINAL ACTIONS & USES Indian snakeroot is useful in the treatment of high blood pressure and anxiety. The root has a pronounced sedative and depressant effect on the sympathetic nervous system. By reducing the system's activity, the herb brings about the lowering of blood pressure. It may also be used to treat anxiety and insomnia, as well as more serious mental health problems such as psychosis. Indian snakeroot is a slow-acting remedy, and it takes some time for its effect to become fully established.
RESEARCH Indian snakeroot and its alkaloids have been extensively researched since the 1930s. Despite concerns raised in the medical journal *The Lancet* in 1974, there is little evidence to show that the root has serious side effects at normal dosage.
RELATED SPECIES The West African species *R. vomitoria* is used as a sedative, aphrodisiac, and anticonvulsant in traditional African medicine.
CAUTIONS Take only under professional supervision. Indian snakeroot is subject to legal restrictions in some countries.

Rhamnus frangula syn. *Frangula alnus*
(Rhamnaceae)
ALDER BUCKTHORN

DESCRIPTION Deciduous shrub or small tree growing to 15 ft (5 m). Has smooth brown bark, oval to elliptical leaves, white flowers, and small round berries ripening from yellow to black.
HABITAT & CULTIVATION Alder buckthorn grows in the northeastern parts of the US and in Europe (except for the Mediterranean region and the extreme north). It prefers marshy woodland. The bark of trees at least 3–4 years old is collected in late spring and early summer, and is dried and stored for at least 1 year before use.
PART USED Bark.
CONSTITUENTS Alder buckthorn contains 3–7% anthraquinones (including frangulin and emodin), anthrones, anthranols, an alkaloid (armepavine), tannins, and flavonoids. The anthrones and anthranols induce vomiting, but the severity of their effect lessens after long-term storage. The anthraquinones found in alder buckthorn and closely related species act on the wall of the colon, stimulating a bowel movement approximately 8–12 hours after ingestion.
HISTORY & FOLKLORE Common buckthorn (*R. catharticus*), a related plant with similar medicinal properties, "purgeth downwards both choler and flegm, and the watery humors of such as have the dropsie, and strengtheneth the inward parts again by binding," according to the 17th-century herbalist Nicholas Culpeper.
MEDICINAL ACTIONS & USES Alder buckthorn is a laxative and a cathartic, and is most commonly taken as a treatment for chronic constipation. Once dried and stored, it is significantly milder than senna (*Cassia senna*, p. 72) or common buckthorn (*R. catharticus*) and may be safely used over the long term to treat constipation and to encourage the return of regular bowel movements. Alder buckthorn is a particularly beneficial remedy if the muscles of the colon are weak and if there is poor bile flow. However, the plant should not be used to treat constipation resulting from excessive tension in the colon wall.
RELATED SPECIES Cascara sagrada (*R. purshiana*), which is native to Pacific North America, is used much like alder buckthorn. Common buckthorn, a European native, is today used mainly in veterinary medicine.
CAUTIONS Use only dried bark that has been stored for at least a year, since the fresh bark is violently purgative. The berries may also be harmful if eaten.



ALDER BUCKTHORN bark is toxic when fresh but is safe to use once dried and stored for a year.