Lech Wojciech Szajdak
Editor

Bioactive Compounds in Agricultural Soils

Springer

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Chapter 11
Cranberry: A Plant Growing on Organic Soils with a Broad Spectrum of Pharmaceutical and Medical Use

Lech Wojciech Szajdak and Lydia I. Inisheva

Abstract Cranberry is a significant example of a plant which is growing on peat soils and has a high content and a rich spectrum of biologically active substances. The organic compounds in the plant are responsible for its wide medical and pharmaceutical use. The beneficial impact of cranberries on human health is caused by the presence of the following substances in the berries: anthocyanins, proanthocyanidins (condensed tannins), flavonol glycosides, low-molecular-weight phenolic acids, organic acids, and sugars. Cranberry juice and fruits are reported to display a number of health benefits including: potent antioxidant activity, cholesterol reduction, vasorelaxant effects, the prevention of urinary tract infections, the reduction of biofilm formation, and in vivo anticancer effects.

Keywords Cranberry • Biologically active substances • Health benefits

11.1 Introduction

Cranberry was introduced to the Western civilization by the pilgrims of Plymouth Colony. For numerous centuries it was used as a staple ingredient of pemmican—a mixture of dried venison, fat, and cranberries—by the indigenous peoples of America inhabiting the Northern Atlantic Coastal Plain. Growers have breeded a group of high-quality cultivars of the original *Vaccinium macrocarpon*. Cranberry is a unique fruit requiring a high level of horticulture. It demands an acid peat soil (pH 4–6) and grows in natural forest pockets. It can be easily damaged by trampling or

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improper drainage. These factors make cranberry growing a difficult and a high-risk endeavor.

Unlike most other crop systems, cranberry growing is a form of swamp agriculture. Successful water management is the *sine qua non* of cranberry breeding. Bog or marsh sites are chosen with consideration of air drainage, water drainage, and water availability. The establishment of an entire complex of reservoirs, dikes, ditches, trunks, and bogs has only one aim: a precise control of water distribution (Brick 1980).

Cranberry—*Vaccinium macrocarpon Ait*—is a creeping evergreen shrub which is both cultivated and wild harvested. Cranberries are characteristic of boreal landscape and organic soils—peat soils—where climate is severe. The plants are native to acidic bogs and peat wetlands as they favor acidic conditions.

Cranberry can grow and survive only when certain conditions are met. These include acidic peat soil, an adequate fresh water supply, and a growing season extending from April to November. Cranberries grow on low-lying vines in beds layered with sand, peat, gravel, and clay. These beds were originally created by glacial deposits and are commonly known as bogs or marshes. Commercial bogs use a system of wetlands, uplands, ditches, flumes, ponds, and other water bodies that provide a natural habitat for a variety of plant and animal life (Brick 1980).

In 2004, according to FAO report, the world production of cranberry amounted to 757 million pounds. Some analysts predict that the world production will rise by ca, 40 % over the period of 2013–2018, surpassing the one million tons mark by 2018.

The production of cranberry is mostly limited to the Northern USA and Canada, which are at the top of world production of this plant—82 % and 14 %, respectively. The production of cranberries in other countries is significantly lower than in the USA or Canada: Latvia 2 %, Belarus <1 %, Azerbaijan <1 %, Ukraine <1 %, and Estonia <1 %.

Cranberries are one of the very few crops that are native to the USA. The USDA National Agricultural Statistics Service released its projected yields for the 2014 season. The total USA cranberry production was estimated to be 8.72 million barrels (a barrel is 100 pounds of cranberries). Wisconsin, which produces 57 % of the country's yields, was predicted to yield 4.5 million barrels, up 2 % from 2011. Massachusetts was forecasted to produce 2.10 million barrels, down 9 % from 2011. New Jersey was going to yield 542,500 barrels; Oregon, 400,000 barrels; and Washington, 142,000 barrels. The average yield in 2014 was 211.6 barrels per acre nationwide, an increase of 0.2 barrels per acre in comparison with 211.4 barrels in 2013. Approximately ten million barrels are produced globally, including the production in the USA, Canada, and Chile.

11.2 Methods

pH Instrument, pH meter; reagent, 0.1 N KCl

pH of peat was assayed potentiometrically in 1 N KCl (1:2.5, v/v) suspensions using combination electrode.

The Determination of Total Nitrogen The total nitrogen was estimated by Kjeldahl method.

The Determination of Total Organic Carbon The total organic carbon was estimated by TOC 5050A with Solid Sample Module, SSM-5000A, Shimadzu, Japan.

The Determination of Dissolved Organic Carbon For the estimation of dissolved organic carbon (DOC), soil samples in redistilled water were heated at 100 °C during 2 h under reflux condenser. Extracts were separated with the mean filter paper and analyzed on TOC 5050A a facilities (Shimadzu, Japan).

The method of the determination of IAA is described in Chap. 10.

11.3 Conclusions

Peat soils contain a higher concentration of mineral and organic compounds of a well-known and unknown structure than mineral soils. The amount of amino acids, hemicellulose, cellulose, lignin, pectin, bitumens, lipids, waxes, resins, carbohydrates, phenolic compounds, amines, amides, terpenoids, amino sugars, nucleic acids, vitamins, nitrogenous material, non-saturated and saturated fatty acids, organic sulfur compounds, starch compounds, ethereal oils, balsam, antibiotics (streptomycin and penicillin), hormones (derivatives of estrogen), and enzymes is considerable higher in peat soils than in mineral soils. Therefore, peat as a raw material with a rich spectrum of biologically active substances is widely used in agriculture, horticulture, veterinary, pharmacy, and medicine.

Biologically active substances of well-known and unknown structure of peat and peat extracts influence on organisms (Banaszkiewicz and Drobnik 1994; Beer et al. 2003). Peat is involved in the stimulation of digestion as it causes:

(i) The reduction of pH in the intestines
(ii) The contraction of smooth muscles in the gastrointestinal tracts
(iii) The improvement of nutrient uptake and conversion efficiency
(iv) The formation of chelate complexes with heavy metals, toxins produced by pathogenic bacteria, pesticides, etc.
(v) Lipid and protein metabolism

Antibiotics formed by strains of eubacteria and actinomycetes in peat influence the composition of intestinal microflora (Huck et al. 1991). Peat extracts protect

Table 11.1 pH, N-total, dissolve organic carbon (DOC), total organic carbon (TOC), and indole-3-acetic acid (IAA) in soil under cultivation of cranberry (Szajdak, unpublished data)

Time of sampling	pH	N-total	DOC g kg^{-1}	TOC g kg^{-1}	IAA µg kg^{-1}
March 6	6.16	2.10	21.79	475.7	273.20
April 10	5.95	2.29	24.92	434.6	249.45
May 7	5.22	1.80	30.93	433.1	225.69
June 19	5.09	2.40	32.52	450.0	231.63
July 14	5.49	2.01	24.99	473.4	201.93
August 8	5.38	2.30	25.25	472.8	195.99
September 10	5.29	2.22	22.23	451.3	225.69
October 8	5.34	2.45	23.10	450.1	237.57

DOC, dissolved organic carbon; TOC, the total organic carbon; IAA, indole-3-acetic acid

from viral diseases (Klocking and Sprossig 1972; Thiel et al. 1977; Schiller et al. 1979; Sydow et al. 1986; Schols et al. 1991; Jankowski et al. 1993; Laub 2000), activate the immune system (Riede et al. 1991), reduce or minimalize infection in patients (Kuhnert et al. 1982; Pukhova et al. 1987), decrease the total lipid content in liver, and increase leg muscle strength (Stepchenko et al. 1991).

pH of peat soils directly affects the life and growth of plants. pH-dependent processes are important in terms of hydrogen ion equilibrium, stability, ligand interactions, assembly, and dynamics. Therefore, pH affects the availability of all plant nutrients. The nutrients have to be soluble and have to successfully move through the soil solution toward the roots. Nitrogen, for example, has its greatest solubility between soil pH 4–8. Soil microorganisms are involved in the conversion and transformation of chemical and biochemical compounds in soils.

During the entire vegetation seasonal of cranberry, pH values of peat ranged from 5.29 to 6.16 (Table 11.1) (Szajdak, unpublished data).

The concentration of total nitrogen, DOC, and TOC ranged from 1.80 to 2.40% (21.79–32.53 g kg^{-1} and 433.1–475.7 g kg^{-1}, respectively). The highest concentration of IAA was noted in March when it equaled to 273.2 ng kg^{-1}. The content of IAA decreased later during the period of intense plant development. The lowest amount of IAA was determined in August. In autumn the concentration of IAA increased again (Table 11.2). The amount of IAA in Table 11.2 concerns the free form of this compound. Free forms are very unstable and migrate very quickly in soils, IAA physiological function, which expressed by the interaction of IAA with IAA receptor in plants. Therefore, the research on the free form of IAA in fact concerns the biochemical and biological processes in soils.

Cranberry grows in very comfortable conditions of peatlands (Figs. 11.1, 11.2, and 11.3).

The fruit of cranberry has gained significant attention for its putative human health benefits. However, research has mostly been focused on the phenolic acids, their derivatives, and flavonoids due to their high chemical, biological, physiological, and pharmaceutical activity. In vitro chemical analyses showed that cranberries, out of 21 fruits, had the highest antioxidant values (Vinson et al. 2001; Sun et al. 2002).

Table 11.2 Structures of phenolic acids

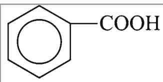
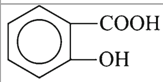
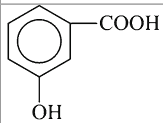
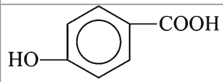
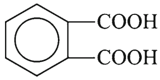
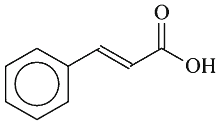
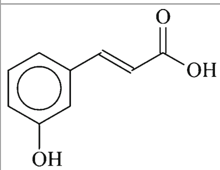
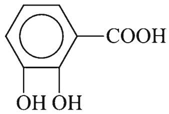
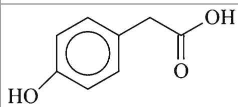
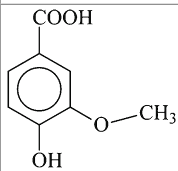
Benzoic acid	
o-Hydroxybenzoic acid	
m-Hydroxybenzoic acid	
p-Hydroxybenzoic acid	
Phthalic acid	
Cinnamic acid	
o-Hydroxycinnamic acid	
2,3-Dihydroxybenzoic acid	
4-Hydroxyphenylacetic acid	
Vanillic acid	

Table 11.2 (continued)

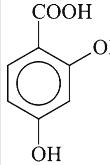
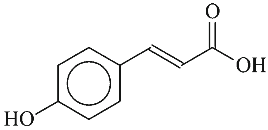
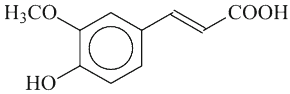
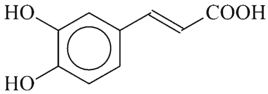
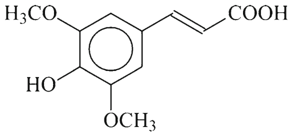
2,4-Dihydroxybenzoic acid	
p-Coumaric acid	
Ferulic acid	
Caffeic acid	
Sinapic acid	

Fig. 11.1 Cranberry cultivation

The overall phenolic content appeared to correlate with the level of antioxidant activity (Vinson et al. 2001; Sun et al. 2002). The phenolic classes identified in cranberry include some phenolic acids (Marwan and Nagel 1982; Heimhuber et al. 1990; Zheng and Shetty 2000; Zuo et al. 2002): anthocyanins (Hong and Wrolstad 1986, 1990), flavonols, procyanidins, proanthoycyanidins, and the derivatives of flavon-3-ols. The derivatives of flavon-3-ols are represented by both monomers and the polymer classes of proanthoycyanidins (Foo and Porter 1981; Foo et al. 2000a, b).

Cranberries are epigynous or "false" berries. The fruit are bright red with waxy bloom at maturity, giving dark red to black appearance. The color changes from green to white and then red during its development. The fruit matures in 60–120

Fig. 11.2 Creeping shrub of cranberry

Fig. 11.3 Mature fruits

days after fertilization, depending on the cultivar and weather. Red color is the primary determinant of harvest maturity and fruit quality. The color increases over time; therefore, harvest is delayed as long as possible to allow color development.

About 90–95 % of the cranberry crop is processed into juices and sauces. Recently, juice blends have become more popular. Cranberry juice and fruits are reported to display a number of health benefits including:

(i) Potent antioxidant activity
(ii) Cholesterol reduction
(iii) Vasorelaxant effects
(iv) The prevention of urinary tract infections
(v) The reduction of biofilm formation
(vi) In vivo anticancer effects

The beneficial impact of cranberries on human health is caused by the presence of the following substances in the berries:

(a) Anthocyanins (Hong and Wrolstad 1990; Mazza and Miniati 1993)
(b) Proanthocyanidins (condensed tannins) (Foo and Porter 1981; Foo et al. 2000a, b) and flavonol glycosides (Puski and Francis 1967)

(c) Low-molecular-weight phenolic acids (Zuo et al. 2002)
(d) Organic acids (Heimhuber et al. 1990)
(e) Sugars (Hong and Wrolstad 1986)

Therefore, the knowledge of bioavailability, the mechanism of uptake, and the consequences of biotransformation of these biologically active substances after cranberry consumption is urgently needed. Incorporating cranberries in a balanced diet rich in fruits, vegetables, and whole grains is recommended for the prevention of cardiovascular disease (CVD). CVD is a major cause of death in most industrialized countries (Chu et al. 2002; Chu and Liu 2005). In the USA, the annual CVD death rate exceeds one million with an annual economic cost evaluated at over 350$ billion, surpassing 3 % of the US GDP (gross domestic product) for a single disease (American Heart Association 2002). Wise diet is said to be an effective method for reducing the formation of artherosclerotic lesions. An increase in fruits and vegetables intake of one daily serving decreases the risk of CVD from 7 to 4 % (Joshipura et al. 2001). Oxidized low-density lipoprotein (LDL) plays a significant role in the initiation and the acceleration of artherosclerotic process. Cardiovascular diseases can be prevented through lowering LDL oxidation.

Cranberries exhibit a very high phytochemical and antioxidant activity (Lusis 2000; Chu et al. 2002; Sun et al. 2002; Liu 2003). Just a single intake of cranberry juice leads to a significant increase in plasma antioxidant level for up to 7 h after the intake. Moreover, it also causes changes in high-density lipoprotein (HDL) in hypercholesterolemic human subjects when consumed for an extended period of time (Miller et al. 1998; Viason et al. 2003). In vitro fresh cranberry extracts inhibited low-density lipoprotein (LDL) oxidation (Wilson et al. 1998), which is a critical point in artherosclerotic conversion (Lusis 2000). The antioxidative activity of 100 g cranberries against LDL oxidation is equivalent to that of 1000 mg vitamin C (ascorbic acid) or 3700 mg vitamin E (tocopherol). Cranberry extracts also significantly induce the expression of hepatic LDL receptors and increase the intracellular uptake of cholesterol in HepG2 cell in vitro in dose-dependent manner. This may suggests that cranberries can clear excessive plasma cholesterol from the vascular system. The pharmacokinetic mechanism is based on the properties of biologically active substances in cranberries. These compounds are responsible for the inhibition of LDL oxidation. They induce the expression of LDL receptors and increase the uptake of cholesterol in hepatocytes (Chu and Liu 2005).

The derivatives of phenolic compounds found in cranberries represent a rich source of natural antioxidants and reveal an inhibitory effect on mutagenesis and carcinogenesis (Rice-Evans et al. 1996; Zuo et al. 2002). Flavonoids and phenolic acids exist in berries predominantly in combined forms, such as glycosides and esters. A total of 400 mg of flavonoids and phenolic compounds (44 %, phenolic acids; 56 %, flavonoids) was found in a freshly squeezed cranberry juice sample. Fifteen benzoic and phenolic acids (benzoic, *o*-hydroxybenzoic, cinnamic, *m*-hydroxybenzoic, *p*-hydroxybenzoic, *p*-hydroxyphenyl acetic, phthalic, 2,3-dihydroxybenzoic, vanillic, *o*-hydroxycinnamic, 2,4-dihydrobenzoic, *p*-coumaric, ferulic, caffeic, and sinapic) were identified in cranberry fruit in their free and bound forms. Cranberry fruit contained a high amount of benzoic and phenolic acids (5.7 g/kg fresh weight) with benzoic acid being the most abundant (4.7 g/kg fresh weight) (Table 11.2).

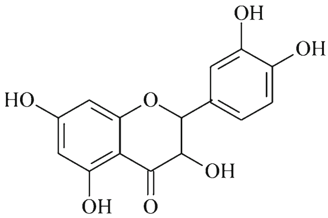
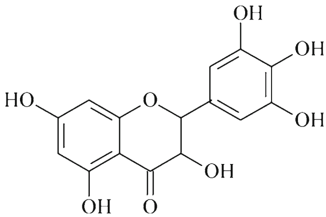
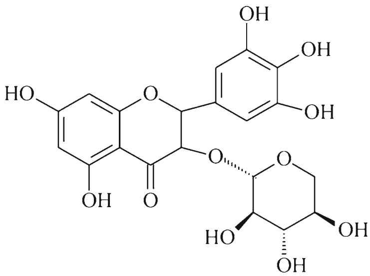
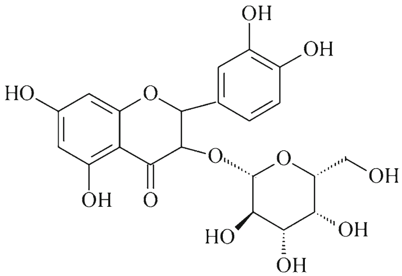
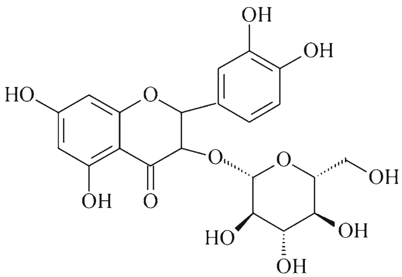
Benzoic and phenolic acids occur mainly in bound forms, while only about 10 % of them occur as free acids. What is more, a cranberry fruit included *p*-coumaric (0.25 g/kg fresh weight) and sinapic acids (0.21 g/kg fresh weight). Quercetin and myricetin were the most common flavonoids found in the freshly squeezed cranberry juice. In addition, the derivatives of flavonol glycoside conjugates were represented by quercetin-3-α-arabinopyranoside, quercetin-3-*O*-(6″-*p*-coumaroyl)-*β*-galactoside, 3′-methoxyquercetin-3-α- xylopyranoside, myricetin-3-*β*-xylopyranoside, and quercetin-3-*β*-glucoside (Vvedenskaya et al. 2004) (Table 11.3).

It has been well established that complex biologically active substances in cranberry fruit can provide protective health benefits mainly through a combination of additive and/or synergistic effects. These substances can have a complementary and overlapping influence on oxidative stress, the immune system, gene expression in cell proliferation and apoptosis, and hormone metabolism. They can also have a direct antibacterial and antiviral effect. In addition, cranberries inhibit the development of tumor cells in oral, prostate, and colon cancer patients (Yan et al. 2002; Vaisberg and Neto 2003; Seeram et al. 2004).

Moreover, recent studies indicate that cranberry extracts exhibit antimicrobial activity against several food-borne and human pathogens (Cavanagh et al. 2003; Vattem et al. 2005). They also inhibit the adhesion of *Helicobacter pylori* to the gastric mucus. *Helicobacter pylori* is a “Gram-negative” microaerophilic bacterium that lives in the stomach and duodenum. Infections caused by *Helicobacter pylori* are generally recognized as one of the etiological agents of gastritis, peptic ulcer, gastric cancer, mucosa-associated lymphoid tissue lymphoma (Uemura et al. 2001; Fox and Wang 2001), and cardiovascular diseases (Pellicano et al. 2003). Helicobacter pylori is indigenous to the stomach of more than 50 % of the entire population, reaching 80 % in some countries (Dunn et al. 1997; Vattem et al. 2005). Most chronic infections caused by *Helicobacter pylori* are asymptomatic, and only if the colonization of the bacteria persists, symptoms appear in 15–20 % of the infected population (Parsonnet et al. 1991). Dietary management of *Helicobacter pylori* infection by consuming fruits of cranberries and their products could be an effective strategy due to likelihood of high compliance and absence of side effects.

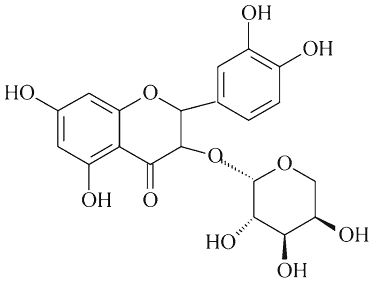
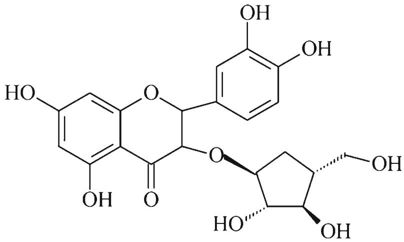
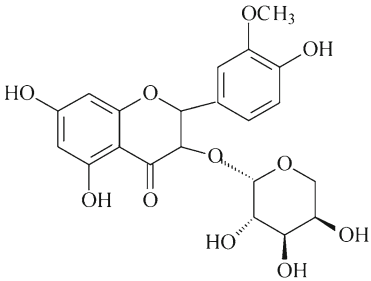
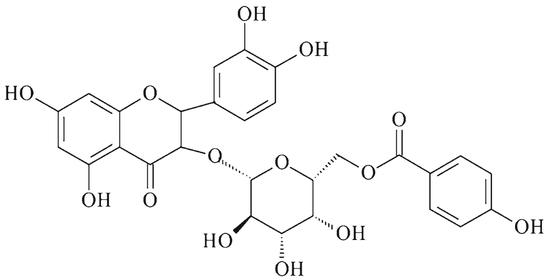
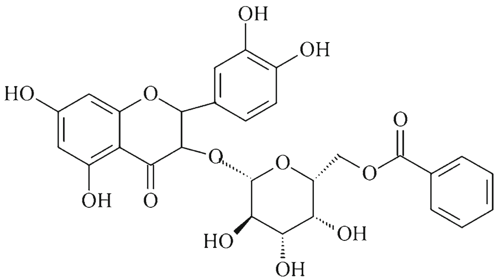
Clinical studies also confirm that cranberries have a beneficial impact on the prevention of urinary tract infections (Kontiokari et al. 2001; Stothers 2002; Howell et al. 1998, 2005). The adhesion of microorganisms to the uroepithelium is the initial step in the development of mammalian urinary tract infections. Cranberry may inhibit the adhesion of P-fimbriated uropathogenic strains of *Escherichia coli* to uroepithelial cells (Ofek et al. 1991). *Escherichia coli* strains that express P-fimbriae are linked to both cystitis and pyelonephritis (Roberst et al. 1989). The majority of P-fimbriated *Escherichia coli* that cause a urinary tract infection bind glycosphingolipid receptor sites on the uroepithelium that are similar in structure to the P blood group antigens on the surface of A_1, Rh+human red blood cells (Kallenius et al. 1980).

Table 11.3 Structures of quercetin and myricetin and flavonol glycosides isolated from cranberry (Vvedenskaya et al. 2004)

Quercetin	
Myricetin	
Myricetin-3-β-xylopyranoside	
Quercetin-3-β-galactoside	
Quercetin-3-β-glucoside	

(continued)

Table 11.3 (continued)

Quercetin-3-α-arabinopyranoside	
Quercetin-3-α-arabinofuranoside	
3′-Methoxyquercetin-3-α-xylopyranoside	
Quercetin-3-O-(6″-p-coumaroyl)-β-galactoside	
Quercetin-3-O-(6″-benzoyl)-β-galactoside	

Proanthocyanidins isolated from cranberry inhibit P-fimbrial adhesion in vitro and, thus, may be able to prevent urinary tract infections (Howell et al. 1998, 2005).

Cranberries are also an excellent dietary source of a wide array of phytochemicals of physiological significance, which include:

(i) Flavonol glycosides
(ii) Anthocyanins
(iii) Proanthocyanidins
(iv) Organic and phenolic acids

Cranberry juice and fruit exhibit various health benefits. Numerous studies have shown that cranberries display potent antioxidant activity. Moreover, they reduce cholesterol and biofilm formation and prevent urinary tract infections. Furthermore, cranberries are reported to have vasorelaxant and in vivo anticancer effect.

Cranberry is a significant example of a plant which is growing on peat soils and has a high content and rich spectrum of biologically active substances. The organic compounds in the plant are responsible for its wide medical and pharmaceutical use.

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