International Journal of Chemistry, Pharmacy & Technology
Vol. 2, No.1, pp-25-33, 2017

A REVIEW ON POTENTIAL DIETARY HEALTH BENEFIT OF FLAVONOIDS

Kumud Upadhyaya[2], Bhawana Saini[1] and Praveen Kumar Ashok[1]*

[1]Department of Pharmacy, GRD (PG) IMT, 214, Rajpur Road, Dehradun.
[2]Department of Pharmaceutical Science, Kumaun University, Bhimtal, Nainital.
Corresponding Author: pkashok157@gmail.com
Received 24-01-17; Revised & Accepted: 09-02-17

ABSTRACT

Flavonoids are low molecular weight natural products. Flavonoids absorb the harmful ultraviolet radiation. They are found in fruits, vegetables, nuts, seeds, stems and flowers further as tea, wine propolis. Flavonoids are a very large group of polyphenolic natural products. The fundamental structural feature of flavonoid compounds is the presence of 2-phenyl-benzo[α]pyrane or flavone nucleus. Flavonoids are known to be very powerful antioxidant; they prevent the degradation caused to body cells by the free radicals and thus positive for our health. Flavonoids determination is done by using Aluminum chloride colorimetric method. The major flavonoids component quercetin is helpful in some of the allergies like hay fever, hives, etc. It inhibits the production and release of histamine and different allergic/inflammatory substances possibly by stabilizing cell membranes of mast cells. To date, more than 6000 different flavonoids have been identified and the number continues to increase. The recently increase in consumer awareness on the health benefits of dietary phytochemicals accompanied by the rapid progress in the field of molecular biology has provided the means and incentive to enhance the functional value of plant material.

Keywords: Antioxidant, Flavonoids, Phytochemicals

INTRODUCTION

Flavonoids are a broad class of low molecular weight, secondary plant phenolics characterized by the flavon nucleus. Widely distributed in the leaves, seeds, bark and flowers of plants, to date over 4,000 flavonoids have been identified. In plants, these compounds afford protection against ultraviolet radiation, pathogens, and herbivores. The anthocyanin co-pigments in flowers attract pollinating insects [1] and are responsible for the characteristic red and blue color of berries, wines, and certain vegetables and major sources of flavonoids in the human diet [2,3].

Most dietary flavonoids occur in food as *O*-glycosides. The most common glycosidic unit is glucose, but other examples include glucorhamnose, galactose, arabinose, and rhamnose. Flavonoids protect plants against various biotic and abiotic stresses, exhibit a diverse spectrum of biological functions, and play an important role in the interaction between plant and their environment [4]. Flavonoids absorbe the harmful UV radiation induced cellular damage [5]. Flavonoids are not essential for plant survival; nevertheless, they are bioactive and influence the

transport of the plant hormone, auxin [6]. Flavonoids are responsible for flower colors, protecting the plants from microbes and insects [7-9].

Flavonoids exhibit several biological effects such as anti-inflammatory, anti-hepatotoxic and anti-ulcer actions [10, 11]. They also inhibit the enzymes such as aldose reductase and xanthine oxidase. They are potent antioxidants and have free radical scavenging abilities. Flavonoids are reported have anti-allergic, antiviral actions and some of them provide protection against cardiovascular mortality [12, 13].

FLAVONOIDS: OCCURRENCE, FUNCTIONS, AND STRUCTURE

Flavonoids are ubiquitous in photosynthesizing cells, and therefore occur widely in the plant kingdom [14]. They are found in fruit, vegetables, nuts, seeds, stems and flowers as well as tea, wine [15] propolis and honey [16] and represent a common constituent of the human diet [17]. In US the daily dietary intake of mixed flavonoids is estimated to be 1000 mg, but this figure can be higher in people supplementing their diets with flavonoids or flavonoid-containing herbal preparations [18].

OCCURRENCE OF FLAVONOIDS IN FOOD [19, 20]

S. No.	Flavonoid subclass	Food source	Representative Flavonoids
1.	Flavonol	Onion, kale, broccoli apples, cherries, berries, tea, red wine	Kaempherol, myricetin, quercetin, rutin
2.	Flavones	Parsley, Thyme	Apigenin, chrysin, luteolin
3.	Flavonones	Citrus	Hesperitin, erodictyol, naringen
4.	Catechins	Apple, tea	Catechin, galocatechin
5.	Anthocyanidins	Cherries, Grapes	----------
6.	Isoflavones	Soya beans, Legumes	Daidzen, genistein, glyciten, formanantine

The function of flavonoids in flowers is to provide colour attractive to plant pollinators [21]. In leaves, these compounds are believed to promote physiological survival of the plant, protecting it from fungal pathogens and UV- radiation. In addition, flavonoids are involved in photosensitization, energy transfer, actions of plant growth hormones and plant growth regulators, control of respiration, photosynthesis, morphogenesis and sex determination.

The basic structural feature of flavonoid compounds is 2-phenyl-benzo[α]pyrane or flavane nucleus, which consists of two benzene rings (A and B) linked through a heterocyclic pyrane ring (C) [22].

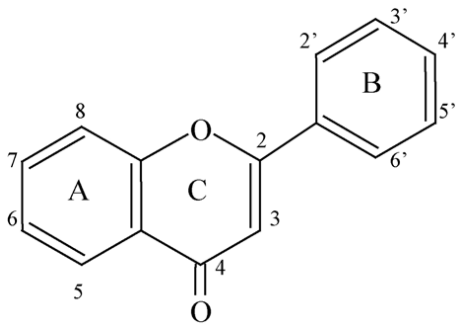

Figure.1 The skeleton structure of the flavones (a class of flavonoids) with rings named and positions numbered

CLASSIFICATION

Flavonoids are a very large group of polyphenolic natural compounds. There are different ways to classify flavonoids, for example, according to their biosynthetic origin, according to whether the central heterocyclic ring is unsaturated or not, according to their molecular size. The most common way is according to the variation of the heterocyclic C ring. From the flavonoid basic structure, a heterocyclic pyrane C ring can be derivatised to the flavones, flavonols, flavanones and isoflavones; a pyrane C ring produces the flavanols and anthocyanins.

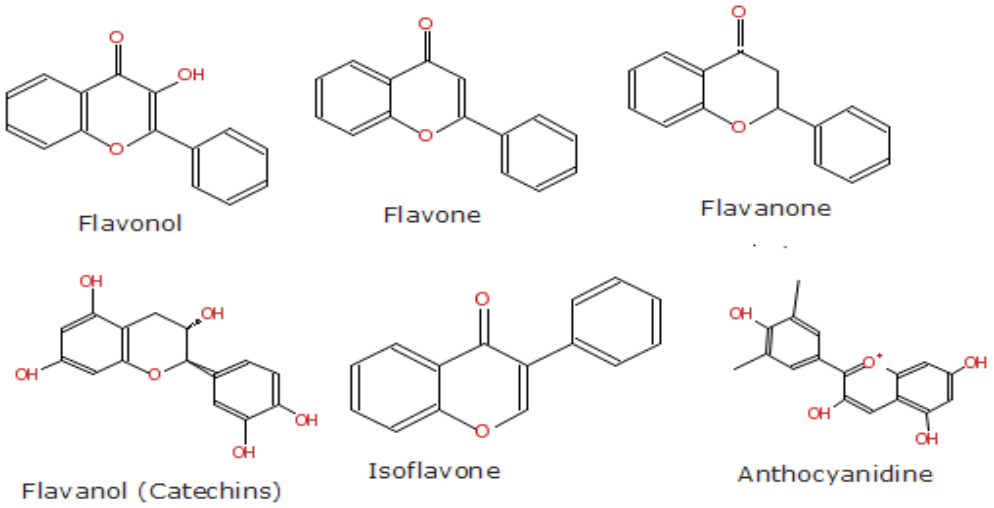

Figure. 2 Structure of the major classes of flavonoids

Flavonoids are mainly divided into six major subgroups [23].

Flavonols

Flavonols are the most commonly found type of flavonoids. They are widely spread in nature and can be found as plant pigments and also in the leaves of Carya Cathayensis. The two main groups of flavonols found in nature are:

- Flavonols: 3-hydroxyflavone, Azaleatin, Fisetin, Galangin, Gossypetin, Kaempferide, Kaempferol, Isorhamnetin, Morin, Myricetin, Natsudaidain, Pachypodol, Quercetin, Rhamnazin, Rhamnetin.
- Flavonols glycosides: Astragalin, Azalein, Hyperoside, Isoquercetin, Kaempferitrin, Myricitrin, Quercitrin, Robinin, Rutin, Spiraeoside, Zanthorhamnin, Amurensin, Icariin and Troxerutin [24].

Flavones

Flavones are found in some herbs and plants but their amounts and occurrence is far from being close to that of Flavonols [25-28].

Flavanones

Flavanones are present in many herbs and fruits, but among the entire plant kingdom, the species where flavanones are most commonly found in citrus. Citrus contain a significantly big amount of flavanone, being the richest source of flavanones, especially when they are still immature [29-30].

Flavan-3-ols

Onions are a great source of flavan-3-ols. Quercetin, a well known flavan-3-ols, is used to treat allergies. Cacao is another source of flavan-3-ols, containing other types of flavan-3-ols as chatechins and epicatechins [31-34].

Isoflavones

Isoflavones are mainly present in the Leguminosae family; soybean sprouts being a very good source of isoflavones [35-38].

Anthocyanidin

These are the most abundant type of flavonoid and they are responsible for the blue or purple colour present in blueberries, cherries, grapes, blackberries and others. Actually a little bit more than 500 anthocyanidins have been found in different herbs, plants and natural sources [39-45].

TEST FOR FLAVONOIDS [46-48]

Shinoda test

Crude extract is mixed with few fragments of magnesium ribbon and concentrate HCl is added drop wise. Pink scarlet colour appeared after few minutes, which indicated the presence of Flavonoids.

Alkaline reagent test

Crude extract is mixed with 2ml of 2% solution of NaOH. An intense yellow colour is formed which becomes colorless on addition of few drops of dilute acid which indicates the presence of flavonoids.

Determination of Total Flavonoids

Aluminum chloride colorimetric method was used for flavonoids determination. Each plant extracts (0.5 ml of 1:10 g ml^{-1}) in methanol is separately mixed with 1.5 ml of methanol, 0.1 ml of 10% aluminum chloride, 0.1 ml of 1 M potassium acetate and 2.8 ml of distilled water. It is kept at room temperature for 30 min; the absorbance of the reaction mixture is measured at 415 nm with a double beam UV/Visible spectrophotometer. The calibration curve is prepared by preparing quercetin as standard solutions at concentrations 12.5 to 100 g ml^{-1} in methanol [49].

USES

Flavonoids are documented as a cancer preventive agent and an many useful active constituent of herbs and plants responsible for several useful properties of these ones, as their anti-ageing effect (Ginkgo biloba, calendula etc.) and their free radical scavenging action (antioxidant), preventing cancer occurrence. Flavonoids are familiar to be better-known powerful antioxidant; they avoid the degradation caused to body cells by the free radicals, thus thought to be positive for our health [50-52].

The flavonoid quercetin is reported to anti-inflammatory activity. Quercetin, kaempferol, Morin, myricetin and rutin, by acting as antioxidants exhibited beneficial effects, such as anti allergic, antiviral as well as anticancer activity [53-54].

The properties of flavonoids to absorb ultraviolet radiation builds flavonoid as a very useful remedy against the damage caused to our DNA by daylight and different ultraviolet radiation light sources. This might facilitate preventing carcinoma and different skin disorders associated with the damage caused to DNA by ultraviolet radiation [55]. Quercetin is found to be a substance of the enzyme

aldose reductase that plays a role in converting aldohexose (sugar) to sorbitol (a sugar alcohol) within the body. People with diabetes develop secondary issues, like neuropathy, retinopathy, diabetic cataracts, and nephropathy as a result of sorbitol buildup within the body. Quercetin could thus be useful within the nutritional management of diabetes; however clinical studies have to be compelled to be conducted to verify these effects that are determined in non- human experiments [56-57]. The dark berries are known to be rich in flavonoids, as well the already mentioned apple, the strawberries and black tea or blueberries. It seems that those flavonoids found in berries may have a positive effect and protect against Parkinson's disease. [58-59].

Flavonoids in treatment of Cancer: Flavonoids for an extended time are a part of the herbal treatment by lay practitioners, however they were recognized only recently as effectors substances. Examples of herbal preparations owing their growing recognition as effective anticancer drugs to flavonoids are propolis and Essiac [60].

Flavonoids have also been shown to possess regulatory activity of hormones, by binding to 17 beta-hydroxyl steroid dehydrogenases that regulates sex hormone and estrogen levels in humans and to 3 beta-hydroxyl steroid dehydrogenase that regulates progestin and androgen levels in humans. Quercetin could be helpful in some of the allergies like hay fever, hives. It inhibits the production and release of histamine and different allergic/inflammatory substances possibly by helpful cell membranes of mast cells [61-62]. Flavonoids may play a role in the prevention and/or treatment of the following health condition:

Allergy, Asthma, Atopic dermatitis, Candida infection, Cataracts, Diabetes, Gout, Hemorrhoids, Macular degeneration, Migraine, Periodontal

REFERENCES

[1] Harborne JB, Williams CA, Advances in flavonoid research since 1992, Phytochemistry, 2000, 55, 481–504.

[2] Hammerstone JF, Lazarus SA, H H, Schmitz J, Nutr Procyanidin content and variation in some commonly consumed foods. 2000, 130, 2086S–2092S.

[3] Reinli K, Block G, Phytoestrogen content of foods: a compendium of literature values, Nutr Cancer IntJ, 1996, 26, 123–148.

[4] Pourcel L, Routaboul JM, and Cheynier V, Flavonoid oxidation in plants: from biochemical properties to physiological functions. Trends Plant Sci, 2007, 12(1), 29-36.

[5] Takahashi A, Ohnishi T, The significance of the study about the biological effects of solar ultraviolet radiation using the exposed facility on the internal space station. Biol. Sci. Space, 2004, 18(4), 255-260.

[6] Buer CS, Imin N, Djordjevic MA, Flavonoids: New roles for old molecules. J. Integrative Plant Biol, 2010, 52(1), 98-111.

[7] Griesbach RJ, Biochemistry and genetics of flower color. Plant Breed, Rev., 2005, 25, 89-114.

[8] Bohm BA, Introduction to flavonoids. Amsterdam, The Netherlands, Hardwood academic publishers, 1998, 365-394.

[9] Yao LH, Jiang YM, Shi J, Flavonoids in Food and Their Health Benefits. Plant Foods Hum. Nutr. (Formerly QualitasPlantarum), 2004, 59, 113-122.

[10] Bors W, Heller W, Michel C, Saran M, Flavonoids as anti- oxidants: Determination of radical scavenging efficiencies. Methods Enzymol, 1990, 186, 343-355.

[11] Colerige Smith PO, Thomas P, Scurr JH, Dormandy JA, Causes of various ulceration, a new hypothesis. Br Med j, 1980, 296, 1726-1737.

[12] Clack W, Mackay E, Effect of flavonoid substances on his- tamine toxicity, anaphylactic shock and histamine enhanced capacity to dye. J Allergy, 1950, 21, 133-147.

[13] Hertog MGL, Hollman PCH, Katan MB, KIomhout D, In- take of potentially anticarcinogenic flavonoids and their de- terminants in adults in the Netherlands. Nutr Cancer, 1993, 20:21-29.

[14] Havsteen B, Flavonoids, a class of natural products of high pharmacological potency.Biochem Pharmacol, 1983, 32, 1141–1158.

[15] Middleton Jr E, Chithan K, The impact of plant flavonoids on mammalian biology: implications for immunity, inflammation and cancer. In: Harborne JB, editor. The flavonoids: advances in research since 1986. London, UK: Chapman and Hall.

[16] Grange JM, Davey RW, Antibacterial properties of propolis (bee glue). J R Soc Med, 1990, 83, 159–160.

[17] Harborne JB, Baxter H, The handbook of natural flavonoids, Vol, 1 and 2.Chichester, UK: John Wiley and Sons,1999.

[18] Skibola CF, Smith MT, Potential health impacts of excessive flavonoid intake. Free RadicBiol Me, 2000, 29, 375–383.

[19]. Hollman, PCH, Katan, MB, Dietary Flavonoids: Intake, Health Effects and Bioavailability. Food and Chemical Toxicology, 1999, 37, 937-942.

[20]. Ren, W, Qiao, Z, Wang, H, Zhu, L, Zhang, L, Flavonoids: Promising Anticancer agents. Medicinal Research Reviews, 2003, 23, 519-534.

[21] Harborne JB, Williams CA, Advances in flavonoid research since 1992. Phytochemistry, 2000, 55, 481–504.

[22] Brown JP, A review of the genetic effects of naturally occurring flavonoids, anthraquinones and related compounds.MutatRes, 1980, 75, 243–277.

[23] Molecular structures of major classes of flavonoids retrieved from http://www.emolecules.com/cgi-bin/search.

[24] Mullen W, Boitier A, Stewart AJ, Crozier A. Flavonoid metabolites in human plasma and urine after the consumption of red onions: Analysis by liquid chromatography with photodiode array and full scan tandem mass spectrometric detection. J Chromatogr A, 2004, 1058,163–168.

[25] Crozier A, Ashihara H, Clifford MN (Eds). Plant Secondary Metabolites and the Human Diet. Oxford: Blackwell Publishing, 2006a.

[26] Llorach R, Martinez-Sanchez A, Tomas-Barberan FA, Gil MI, Ferreres F. Characterisation of polyphenols and antioxidant properties of five lettuce varieties and escarole Food Chem, 2008, 108,1028–38.

[27] Crozier A, Yokota T, Jaganath IB, Marks SC, Saltmarsh M, Clifford MN. Secondary metabolites in fruits, vegetables, beverages and other plant-based dietary components. In: Crozier A, Ashihara H, Clifford MN, Eds. Plant Secondary Metabolites and the Human Diet. Oxford: Blackwell Publishing, 2006b, 208–202.

[28] Herrmann K. Flavonols and flavones in food plants: A review. J Food Technol, 1976, 11:433–448.

[29] Manach C, Scalbert A, Morand C, Re´me´sy C, Jimenez L. Polyphenols: Food sources and bioavailability. Am J Clin Nutr, 2004, 79:727–747.

[30] Toma´ s-Barbera´n FA, Clifford MN. Dietary hydroxybenzoic acid derivatives— nature, occurrence and dietary burden. J Sci Food Agric, 2000, 80:1024–1032.

[31] Aron PM, Kennedy JA. Compositional investigation of phenolic polymers isolated from Vitis vinifera L. cv. Pinot Noir during fermentation. J Agric Food Chem, 2007, 55:5670–5680.

[32] Crozier A, Jaganath IB, Clifford MN. 2006b. Phenols, polyphenols and tannins: An overview. In: Crozier A, Ashihara H, Clifford MN, Eds. Plant Secondary Metabolites and the Human Diet. Oxford: Blackwell Publishing, 2006c, 1–31.

[33] Gu L, Kelm MA, Hammerstone JF, Beecher G, Holden J, Haytowitz D, Gebhardt S, Prior Rl. Concentration of proanthocyanidins in common foods and estimates of normal consumption. J Nutr, 2004, 134:613–617.

[34] Auger C, Al Awwadi N, Bornet A, Rouanet JM, Gasc F, Cros G, Teissedre P L. Catechins and procyanidins in Mediterranean diets. Food Res Int, 2004, 37:233–245.

[35] Graham TL. Flavonoid and isoflavonoid distribution in developing soybean seedling tissues and in seed and root exudates. Plant Physiol, 1991, 95:594–603.

[36] Dixon RA, Steele CL. Flavonoids and isoflavonoids—a goldmine for metabolic engineering. Trends Plant Sci, 1999, 4:394–400.

[37] Coward L, Smith M, Kirk M, Barnes S. Chemical modification of isoflavones in soyfoods during cooking and processing. Am J Clin Nutr, 1998, 68:14865–14915.

[38] Dewick PM. Isoflavonoids. In: Harborne JB, Ed. The Flavonoids: Advances in Research Since 1986. London: Chapman and Hall, 1993, 117–238.

[39] Prior RL, Wu X. Anthocyanins: Structural characteristics that result in unique metabolic patterns and biological activities. Free Rad Res, 2006, 40:1014–1028.

[40] Kong JM, Chia LS, Goh NK, Chia TF, Brouillard R. Analysis and biological activities of anthocyanins. Phytochemistry, 2003, 64:923–933.

[41] Mazza G, Miniati E. Anthocyanins in Fruits, Vegetables and Grains. Boca Raton, FL: CRC Press, 1993.

[42] Burns J, Gardner PT, Matthews D, Duthie, GG, Lean MEJ, Crozier A. Extraction of phenolic compounds and changes in antioxidant activity of red wines during vinification. J Agric Food Chem, 2001, 49:5797–5808.

[43] Gil MI, Toma´ s-Barbera´n FA, Hess-Pierce B, Holcroft DM, Kader AA. Antioxidant activity of pomegranate juice and its relationship with phenolic composition and processing. J Agric Biol Chem, 2000, 48:4581–4589.

[44] Donner H, Gao L, Mazza G. Separation and characterization of simple and malonylated anthocyanins in red onions. Allium cepa L. Food Res Int, 1997, 30:637–643.

[45] Ferreres F, Gil MI, Castan˜ er M, Toma´ s-Barbera´n FA. Phenolic metabolites in red pigmented lettuce (Lactuca sativa). Changes with minimal processing and cold storage. J Agric Food Chem, 1997, 45:4249–4254.

[46] Sofowra, A, Medicinal Plants And traditional Medicine in Africa. Spectrum Books Ltd., Ibadan, Nigeria, 1993, 191-289.

[47] Trease, GE, Evans, W C, Pharmacognosy, 11th edn.,BailliereTindall, London, 1989, 45-50.

[48] Harborne, JB,Phytochemicals Methods.Chapman andHall Ltd., London, 1973, 49-188.

[49] Chang C, Yang M, Wen H, Chern J, Estimation of total flavonoid content in propolis by two complementary colorimetric methods. J. Food Drug Analaysis, 2002, 178-182.

[50] Liu S, Manson JE, Lee IM, Cole SR, Hennekens CH, Willett WC, Buring JE. Fruit and vegetable intake and risk of cardiovascular heart disease: The Women's Health Study. Am J Clin Nutr, 2000, 72:922–928.

[51] Chan MM, Mattiacci JA, Hwang HS, Shah A, Fong D. Synergy between ethanol and grape polyphenols, quercetin, andresveratrol, in the inhibition of the inducible nitric oxide synthase pathway. Biochem Pharmacol, 2000, 60:1539–1548.

[52] Lee WK, Lee HJ. The roles of polyphenols in cancer chemoprevention. Biofactors, 2006, 26:105–121.

[53] Santos AC, Vyemura SA, Lopes JL, Bazon JN, Mingatto FE, Curtic. Effect of naturally occuring flavonoids on lipid peroxidation and membrane permeability transition in mi- tochondria. Free Radicchio Med, 1998, 24, 1455-1461.

[54] Fraga CG, Mactino US, Ferraro GE, Coussio JF, Boveris A, Flavonoids as antioxidants evaluated by in vitro and in situ liver chemiluminescence. Biochem Med MetabolBioI, 1987, 36, 717-720.

[55] Langcake P, Pryce RJ. The production of resveratrol and viniferins by grapevines in resposne to ultraviolet radiation. Phytochemistry, 1977, 16:1193–1196.

[56] WHO. Diet Nutrition and the Prevention of Chronic Diseases, Report of a Joint WHO/FAO Expert Consultation, WHO Technical Report Series 916. Geneva, World Health Organization, 2003.

[57] Riboli E, Norat T. Epidemiologic evidence of the protective effect of fruit and vegetables on cancer risk. Am J Clin Nutr , 2003, 78:559S–569S.

[58] Mullen W, McGinn J, Lean MEJ, Maclean MR, Gardner P, Duthie GG, Yokota T, Crozier A. Ellagitannins, flavonoids, and other phenolic compounds in red raspberries and their contribution to antioxidant capacity and vasorelaxation properties. J Agric Food Chem, 2002, 50:6902–6909.

[59] Amakura Y, Okada M, Tsuji S, Tonagai Y. High performance liquid chromatographic determination with photo diode array detection of ellagic acid in fresh and processed fruits. J Chromatogr A, 2000, 896:87–93.

[60]. Havsteen, BH, The biochemistry and medical significance of the flavonoids. Pharmacology and Therapeutic, 96, 2002, 167-202.

[61] Lombard KA, Investigation of the flavonolquercetin in onion (Allium cepa L.) by high-performance liquid chromatography (HPLC) and spectrophotometric methodology. M.S. Thesis. Journal of Food Composition and Analysis, 2005, 18, 635-645.

[62] Thornhill SM, Kelly AM, Natural treatment of perennial allergic rhinitis. Alt Med Re, 2005, 5, 448-454.