

A Review on Application of Natural Indicators in Acid-base Titration

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ABSTRACT

Currently, the most usual analytical methods are established to identify compounds, though analytical methods like gravimetry and titrimetric analysis were the most concern. In the titrimetric analysis method, the endpoint is detected by the colour changes from one medium to another medium (either acidic medium or basic medium) with the addition of substances are known as indicators. Nowadays, many synthetic indicators are available, which produce environmental pollution and are costly. Several synthetic indicators produce toxicity in humans. Therefore, the search for alternative indicators from natural sources is required for cost-effectiveness and to minimize the toxicity and pollutant from the environment.

Keywords: Indicator, Natural sources, Phytoconstituents, Synthetic indicator.

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INTRODUCTION

Conventional analytical methods are still appropriate in most applications, including gravimetry and titrimetric analysis. The titrimetric analysis is a quantitative chemical analysis that involves finding the volume of a known concentration solution that reacts quantitatively with a known volume of a solution to the substance to be determined. The equivalency point in titrimetric analysis is usually defined by the detection of the endpoint. The endpoint can be detected by the colour changes from one medium to another medium (either acidic or basic) with the addition of substances which is an indicator.^[1-3] At a specific stage of the chemical reaction, indicators (either weak acid or weak base) change colour. The identification of an acid-base indicator can be represented by a colour change depending on the concentration of Hydrogen (H⁺) or Hydroxide (OH⁻) ions.^[4] Methyl red, methyl orange, phenolphthalein, phenol red, methyl yellow, Penta methoxy red, bromophenol blue, and thymol blue were among the laboratory-based markers.^[5] Natural sources, such as plants,

animals, fungus, and algae, can be used to isolate pigments or dye-based indicators.^[6-8] Sir Robert Boyle first recorded the use of natural dyes in an acid-base indicator in his collection of assays "Experimental History of Colors" in 1664.^[9,10] The various parts of the plant impart colour due to the presence of their extensive distinct character. The number of phytoconstituents including anthocyanins, glucosylated acylated anthocyanin, quinines, anthraquinonoids, naphthoquinones, flavonoids, acylated flavonoids, flavanols, imines, indigoids, polymethines, diarylmethanes, dihydropyrans, and carotene is responsible for the colour property. Among them, flavones are water and alcohol soluble yellow pigments present in plant sources either in a free state or as glycosides or conjugated with tannins. In general, sometimes it is also identified as anthoxanthins (a chemically hydroxylated derivative of flavone). The water-soluble pigment is anthocyanin which is mostly found in flowers, leaves, fruits of the plants. Anthocyanins belong to the class of glycosides, and their aglycones moieties are known as anthocyanidins.^[11] Out of these, some compounds illustrate different colours at different pH levels. As a result, these features in natural substances can be used as an acid-base titration indicator. Nowadays, many synthetic indicators are available that produce pollution to the environment and are not cost-effective.^[12,13] Apart from these, diarrhea, pulmonary oedema, hypoglycemia, pancreatitis, skin rash, eruptions, erythema, and epidermal necrosis are some of the hazardous effects of synthetic indicators.^[14,15] Therefore,



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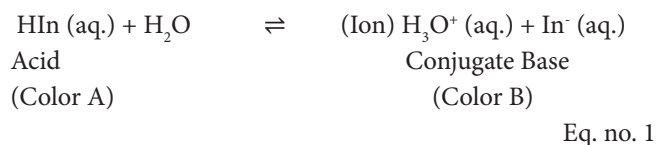
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the gain of the natural-based indicator is an alternative search for the synthetic indicator towards the development of new approaches. These approaches are effective towards the cost, availability, less toxicity and less pollutant for the environment. Furthermore, the most novel outcome of the natural indicators is that they are biodegradable. So, this review aims to highlight the acceptability of some of the natural-based indicators, which is mostly applicable in acid-base titration and to understand the mechanistically based concept of naturally acting indicators.

ACID-BASE INDICATORS AND MECHANISM

Acid-base (pH) indicators are either a weak acid or a weak base that is introduced to a solution in small amounts to visually determine the pH and change colour when the pH changes. In the Arrhenius model,^[16] a pH indicator is a chemical detector for Hydronium Ions (H_3O^+) or Hydrogen Ions (H^+) as shown in the Eq. no. 1. Weak acids or bases that dissociate somewhat when dissolved in water usually serve as indicators. To acquire understanding into the example of a weak acid with the formula HIn as an indicator. With its conjugate base, the following equilibrium equation is established at equilibrium.:



The colours of the acid and its conjugate base are distinct. Because the concentration of H_3O^+ is high at low pH levels, the equilibrium position shifts to the left, becoming colour A. Similarly, the concentration of H_3O^+ is low at high pH levels, and the equilibrium position changes to the right, becoming colour B. A universal indication is a mixture of indicators that gradually change colour over a large pH range; when a few drops of the universal indicator are combined with the solution, the pH of the solution can be approximated. In most titration solutions, indicators are used to mark the conclusion of the acid-based reaction.^[17]

FACTORS INFLUENCING THE COLOUR OF THE INDICATOR

Effect of temperature on the colour of the indicator

The temperature has an impact on the colour-based chemicals' stability. Natural pigments like Curcuma and tulip petals show no colour change at 98°C and 92°C, respectively while borage at 60°C changes red-purple colour.^[18] Studies have revealed that the pH of a solution shows an inversely proportional relationship with temperature except for water. A solution is considered acidic if the excess of hydrogen ions is present over the hydroxide ions. In the case of pure water, the hydrogen and hydroxide

ions concentrations are always the same because of neutral characteristics (even if their pH changes).^[19]

Effect of light on the colour of the indicator

The variation in light's colour composition is evident as white. At midday, sunlight contains nearly equal amounts of all colours. In contrast, the prevalence of colour shifts was seen during daylight. In the early morning, the colour that appears in the presence of light changes considerably.^[20] As a result, the indicator colour must be changed at various time intervals.

NATURAL INDICATOR

Natural-based indicator plays a vital role during titration. Currently, various plants were used as a natural indicator, and their colour changes in a different medium (acidic medium or basic medium) at different pH has listed in Table 1.

COMPOUNDS USED AS A NATURAL INDICATOR

Anthocyanin

The flavonoid anthocyanin has a positive charge oxygen atom on its C-ring. Anthocyanin's stability is affected by pH, light, temperature, and its chemical structure.^[43] On the anthocyanin structure (Figure 1a) at the 7th position, the R group can be incorporated. Various groups such as a methoxyl group, sugar, and other specific substitutions could influence the colouring behaviour of anthocyanin.^[44] Anthocyanin preparation derived from grape juice tanks has been allowed for use in human food, beverage production, and soft drinks, according to the Food Drug and Administration (FDA).^[45]

At low pH, anthocyanins are stable. When subjected to heat, however, it loses its stability, resulting in colour loss and browning. Anthocyanin molecules are present in the equilibrium of a solution between the coloured cationic form and the colourless pseudo base form. pH has a direct impact on this equilibrium, which is critical for the colour of anthocyanins. In acidic solutions, anthocyanins create red, violet or purple in neutral solutions and blue in alkaline solutions. Because anthocyanins have a flavylum cation in their structure, the cyanidin molecule is protonated and produces a cation at low pH. When the pH rises, the molecules deprotonate, and a reaction occurs.^[46,47] The effect of changes in anthocyanin structure based on the surrounding solution and is depicted in Figure 2. Therefore, most of the anthocyanins colourant's can only be used at a pH below four. Additionally, most of the anthocyanin molecules can act as pH indicators in acid-base titration.^[48]

Anthocyanins are primarily found in plants' flowers, fruits, and tubers. The basic colours of anthocyanins are blue, purple, red, and orange, and are determined by the number of hydroxyl groups in the molecule, as well as an indirect relationship with the number of methoxy groups.^[49,50] Red clover, red pineapple sage, red rose, red hibiscus, and pink blossom are examples of red flowers that

Table 1: Plants source used as a natural indicator.

Plants common name	Scientific name	Family	Parts used as an Indicator	Extract name	Name of acid Vs Name of base	Strength in molarity or normality	Indicator colour in acidic medium	Indicator colour in basic medium	pH
Snapdragon ^[21]	<i>Antirrhinum majus</i>	Scrophulariaceae	Flower petal	Methanolic	HCl vs NaOH	1 N	Colourless	Pink	NR
					CH ₃ COOH vs NaOH	1 N	Colourless	Pink	NR
					HCl vs NH ₃	1 N	Colourless	Pink	NR
					CH ₃ COOH vs NH ₃	1 N	Colourless	Pink	NR
Garden Pink ^[21]	<i>Dianthus plumarius</i>	Caryophyllaceae	Flower petal	Methanolic	HCl vs NaOH	1 N	Colourless	Violet	NR
					CH ₃ COOH vs NaOH	1 N	Colourless	Violet	NR
					HCl vs NH ₃	1 N	Colourless	Violet	NR
					CH ₃ COOH vs NH ₃	1 N	Colourless	Violet	NR
Cotton tree ^[22]	<i>Bombax malabaricum</i>	Malvaceae	Flower petal	Methanolic hydrochloric acid	HCl vs NaOH	0.1 N	Green	Colourless	9 - 4.16
						0.5 N			
						1.0 N			
					HCl vs NH ₄ OH	0.1 N	Green	Colourless	8- 4.50
						0.5 N			
						1.0 N			
Flame-of-the-forest ^[23]	<i>Butea monosperma</i>	Fabaceae	Flower petal	Ethanolic	Oxalic acid vs NaOH	0.1 N	Green	Colourless	9-5.22
						0.5 N			
						1.0 N			
					Oxalic acid vs NH ₄ OH	0.1 N	Green	Colourless	8-5.12
						0.5 N			
						1.0 N			
					NaOH vs HCl	0.1 N	Colourless	Yellow	1.68 – 10.75
						0.5 N	Colourless	Yellow	1.03 – 11.72
						1.0 N	Colourless	Yellow	0.77 – 11.78
					HCl vs NH ₄ OH	0.1 N	Yellow	Colourless	10.30 – 2.54
						0.5 N	Yellow	Colourless	10.80 – 2.63
						1.0 N	Yellow	Colourless	11.22 – 2.71
					CH ₃ COOH vs NaOH	0.1 N	Colourless	Yellow	3.67 – 11.41
						0.5 N	Colourless	Yellow	3.00 – 11.50
						1.0 N	Colourless	Yellow	2.46 – 11.43
					CH ₃ COOH vs NH ₄ OH	0.1 N	Colourless	Yellow	3.14 – 7.13
	0.5 N	Colourless	Yellow	2.53 – 7.09					
	1.0 N	Colourless	Yellow	2.36 – 7.01					

continued...

Table 1: Cont'd.

Marigold ^[23]	<i>Calendula officinalis</i>	Compositae	Flower petal	Ethanolic	NaOH vs HCl	0.1 N	Colourless	Yellow	1.57 - 10.67
						0.5 N	Colourless	Yellow	1.1 - 11.65
						1.0 N	Colourless	Yellow	0.67 - 11.68
Wild Guava ^[24]	<i>Careya arborea</i>	Lecythidaceae	Leaf	Methanolic	HCl vs NH ₄ OH	0.1 N	Yellow	Colourless	10.4 - 2.53
						0.5 N	Yellow	Colourless	10.8 - 2.63
						1.0 N	Yellow	Colourless	11.08 - 2.72
					CH ₃ COOH vs NaOH	0.1 N	Colourless	Yellow	3.68 - 11.39
						0.5 N	Colourless	Yellow	3.04 - 10.51
						1.0 N	Colourless	Yellow	2.47 - 10.92
Dahlia ^[25]	<i>Dahlia pinnata</i>	Asteraceae	Flower petals	Methanolic and Aqueous	CH ₃ COOH vs NH ₄ OH	0.1 N	Colourless	Yellow	3.14 - 7.3
						0.5 N	Colourless	Yellow	2.53 - 6.69
						1.0 N	Colourless	Yellow	2.36 - 7.09
Portia tree ^[26]	<i>Thespesia populnea</i>	Malvaceae	Flower petal	Ethanolic	NaOH vs HCl	0.1 M	Yellow	Reddish-brown	6.0-8.0
						0.1 M	Yellow	Reddish brown	6.0-8.0
						0.1 M	Yellow	Reddish-brown	6.0-8.0
Nerium ^[26]	<i>Nerium odorum</i>	Apocynaceae	Flower petal	Ethanolic	NH ₃ vs HCl	0.1 M	Yellow	Reddish-brown	6.0-8.0
					NaOH vs CH ₃ COOH	0.1 M	Yellow	Reddish-brown	6.0-8.0
					NH ₃ vs CH ₃ COOH	0.1 M	Yellow	Reddish-brown	6.0-8.0
Dahlia ^[25]	<i>Dahlia pinnata</i>	Asteraceae	Flower petals	Methanolic and Aqueous	H ₂ SO ₄ vs KOH	0.1 N	orange	Wine red	NR
						0.5 N			
						1.0 N			
Portia tree ^[26]	<i>Thespesia populnea</i>	Malvaceae	Flower petal	Ethanolic	H ₂ SO ₄ vs NH ₄ OH	0.1 N	Pink	Red	NR
						0.5 N			
						1.0 N			
Nerium ^[26]	<i>Nerium odorum</i>	Apocynaceae	Flower petal	Ethanolic	CH ₃ COOH vs KOH	0.1 N	Pink	Yellow	NR
						0.5 N			
						1.0 N			
Portia tree ^[26]	<i>Thespesia populnea</i>	Malvaceae	Flower petal	Ethanolic	CH ₃ COOH vs NH ₄ OH	0.1 N	Orange	Yellow	NR
						0.5 N			
						1.0 N			
Nerium ^[26]	<i>Nerium odorum</i>	Apocynaceae	Flower petal	Ethanolic	NaOH vs H ₂ SO ₄	0.2 M	Pink	Yellow	7.4 - 7.8
						0.2 M	Pink	Colourless	7.0 - 8.6
						0.2 M	Fluorescent yellow	Green	8.8 - 9.0

continued...

Table 1: Cont'd.

Black-eyed Susan vine ^[26]	<i>Thunbergia alata</i>	Acanthaceae	Flower petal	Ethanollic	NaOH vs H ₂ SO ₄	0.2 M	Pink	Green	10.0
Sunflower ^[26]	<i>Helianthus annuus</i>	Asteraceae	Flower petals	Ethanollic	NaOH vs H ₂ SO ₄	0.2 M	Faint blue	Faint yellow	6.6 - 7.0
Hibiscus ^[27]	<i>Hibiscus rosasinensis</i>	Malvaceae	Flower petals	Methanollic	HCl vs NaOH	1.0 N	Pink	Green	NR
					HCl vs NH ₄ OH	0.1 N	Pink	Dark green	NR
					CH ₃ COOH vs NaOH	0.5 N	Pink	Yellow	NR
					CH ₃ COOH vs NH ₄ OH	1.0 N	Pink	Green	NR
Beach Morning Glory ^[28]	<i>Ipomoea biloba</i>	Convolvulaceae	Flower petal	Aqueous	HCl vs NaOH	0.1 N	Pink	Greenish-yellow	NR
					HCl vs NH ₄ OH	0.5 N	Pink	Dark green	NR
					CH ₃ COOH vs NaOH	NR	Pink	Yellow	NR
					CH ₃ COOH vs NH ₄ OH	NR	Pink	Green	NR
					HCl vs NaOH	NR	pink	Green	NR
					HCl vs NH ₃	NR	pink	Green	NR
Jungle geranium ^[29]	<i>Ixora coccinea</i>	Rubiaceae	Flower petal	Methanollic hydrochloric acid	CH ₃ COOH vs NaOH	NR	pink	Green	NR
					CH ₃ COOH vs NH ₃	NR	pink	Green	NR
					HCl vs NaOH	0.1 M	Green	Pink	11 - 4.16
					HCl vs NH ₄ OH	0.5 M	Green	Pink	11 - 4.50
Jacaranda ^[30]	<i>Jacaranda acutifolia</i>	Bignoniaceae	Flower petal	Methanollic hydrochloric acid	Oxalic acid vs NaOH	1.0 M	Green	Pink	11-5.22
					Oxalic acid vs NH ₄ OH		Blue	Pink	11-5.12
					HCl vs NaOH	0.1 M	Green	Colourless	8.9 - 4.12
					HCl vs NH ₄ OH	0.5 M	Green	Colourless	8.2 - 4.34
White mulberry ^[31]	<i>Morus alba</i>	Moraceae	Fruit	Methanollic hydrochloric acid	Oxalic acid vs NaOH	1.0 M	Green	Colourless	9.1-5.35
					Oxalic acid vs NH ₄ OH		Green	Colourless	8.1-5.12
					HCl vs NaOH	0.1 M	Blue	Pink	5.5-8.5
					HCl vs NH ₃	0.5 M	Blue	Pink	5.5-8.5
Pancoli ^[32]	<i>Phyllanthus reticulatus</i>	Euphorbiaceae	Fruit	Ethanollic hydrochloric acid	CH ₃ COOH vs NaOH	1.0 M	Blue	Pink	5.5-8.5
					CH ₃ COOH vs NH ₃		Blue	Pink	5.5-8.5
					NaOH vs HCl	0.1 M	Red	Colourless	NR
					NH ₃ vs HCl	0.5 M	Wine red	violet black	NR
					NaOH vs CH ₃ COOH	1.0 M	Red	Colourless	NR
					NH ₃ vs CH ₃ COOH		Wine red	Violet black	NR

continued...

Table 1: Cont'd.

Pomegranate ^[33]	<i>Punica granatum</i>	Punicaceae	Seed	Methanolic hydrochloric acid	HCl vs NaOH HCl vs NH ₃ CH ₃ COOH vs NaOH CH ₃ COOH vs NH ₃	0.1 M 0.5 M 1.0 M	Pink Pink Pink Pink	Colourless Colourless Colourless Colourless	NR NR NR NR
Beet ^[34]	<i>Beta vulgaris</i>	Amaranthaceae	Root	Ethanol – Hydrochloric acid (v/v ratio 99:1), Ethanol – water (v/v ratio 1: 1)	HCl vs NaOH CH ₃ COOH vs NaOH CH ₃ COOH vs NH ₄ OH HCl vs NH ₄ OH	NR NR NR NR	Pink Pink Pink Pink	Colourless Colourless Colourless Colourless	At P ^H 10
Jambolan ^[35]	<i>Syzygium cumini</i>	Myrtaceae	Fruit peel	Ethanol	NaOH vs HCl 1. Titrant (NaOH) volume 20.50 mL. 2. Titrant (NaOH) volume 21.23 mL.	0.1 M	Pink Pink	Colourless Green	At P ^H 6.25 At P ^H 8.58
					HCl vs NaOH 1. Titrant (HCl) volume 28.60 mL. 2. Titrant (HCl) volume 30.93 mL.		Green Green	Colourless Pink	At P ^H 6.88 At P ^H 3.72
					NaOH vs CH ₃ COOH 1. Titrant (NaOH) volume 21.37 mL. 2. Titrant (NaOH) volume 32.08 mL.		Pink Pink	Green Colourless	At P ^H 8.34 At P ^H 4.26
					HCl vs NH ₄ OH 1. Titrant (HCl) volume 22.13 mL. 2. Titrant (HCl) volume 22.97 mL.		Green Green	Colourless Pink	At P ^H 5.05 At P ^H 3.62
Jacaranda ^[36]	<i>Jacaranda acutifolia</i>	Bignoniaceae	Flower extract	Methanolic hydrochloric acid	HCl vs NaOH HCl vs NH ₄ OH Oxalic acid vs NaOH Oxalic acid vs NH ₄ OH	0.1 M 0.5 M 1.0 M	Green Green Green Green	Colourless Colourless Colourless Colourless	8.9 - 4.12 8.2 - 4.34 9.1-5.35 8.1-5.12

continued...

Table 1: Cont'd.

Morning Glories ^[37]	<i>Ipomea nil</i>	Convolvulaceae	Flower extract	Aqueous	HCl vs NaOH HCl vs NH ₃ CH ₃ COOH vs NaOH CH ₃ COOH vs NH ₃	NR NR NR NR	Pink Pink Pink Pink	Green Green Green Green	NR NR NR NR
Red Onion ^[18]	<i>Allium cepa</i>	Amaryllidaceae	Onion skin	Aqueous	HCl vs NaOH	0.1 M	Purple	Green	NR
Red Cabbage ^[18]	<i>Brassica oleracea</i> var. capitata f. rubra	Brassicaceae		Aqueous	HCl vs NaOH	0.1 M	Red	Purple	NR
Rose ^[38]	<i>Rosa setigera</i>	Rosaceae	Flower	Aqueous	H ₂ SO ₄ vs NaOH CH ₃ COOH vs KOH	0.1 M	Pink Pink	Yellow Yellow	At P ^H 5.50
Turmeric ^[18]	<i>Curcuma longa</i>	Zingiberaceae	Rhizome	Aqueous	HCl vs NaOH	0.1 M	Yellow	Red	NR
Tulip ^[18]	<i>Tulipa gesnerana</i>	Liliaceae	Petals extract	Aqueous	HCl vs NaOH	0.1 M	Red	Purple	NR
Borage ^[18]	<i>Borago officinalis</i>	Boraginaceae	Flower extract	Aqueous	HCl vs NaOH	0.1 M	Colourless	Light Green	NR
Bougainvillea ^[39]	<i>Bougainvillea glabra</i>	Caryophyllales	Flowers petals	Aqueous	NaOH vs HCl NH ₄ OH vs HCl CH ₃ COOH vs NaOH	0.1 M	Red Red Red	Brownish-yellow Brownish-yellow Brownish-yellow	6.0–8.0
Purple orchid tree ^[39]	<i>Bauhinia purpurea</i>	Fabaceae	Flowers petals	Aqueous	NaOH vs HCl NH ₄ OH vs HCl CH ₃ COOH vs NaOH	0.1 M	Red Red Red	Yellow Yellow Yellow	6.0–8.0
Balsam ^[39]	<i>Impatiens balsamina</i>	Balsaminaceae	Flowers petals	Aqueous	NaOH vs HCl NH ₄ OH vs HCl CH ₃ COOH vs NaOH	0.1 M	Red Red Red	Brownish-yellow Brownish-yellow Brownish-yellow	3.4–5.4
Oleander ^[40]	<i>Nerium oleander</i>	Apocynaceae	Flower petals	Ethanol and acetone mixture	HCl vs NaOH	0.1 M	Colourless	Greenish-yellow	NR
Flamboyant ^[40]	<i>Delonix regia</i>	Fabaceae	Flower petals	Ethanol and acetone mixture	HCl vs NaOH	0.1 M	Colourless	Orange-red	NR

continued...

Table 1: Cont'd.

Pumpkin ^[40]	<i>Cucurbita maxima</i>	Cucurbitaceae	Flower petals	Ethanol and acetone mixture	HCl vs NaOH	0.1 M	Colourless	Greenish-yellow	NR
Chinese rose ^[40]	<i>Rosa chinensis</i>	Rosaceae	Flower petals	Ethanol and acetone mixture	HCl vs NaOH	0.1 M	Colourless	Orange-red	NR
Dutchman's pipe ^[40]	<i>Aristolochia littoralis</i>	Aristolochiaceae	Flower petals	Ethanol and acetone mixture	HCl vs NaOH	0.1 M	Colourless	Purplish brown	NR
Allamanda ^[38]	<i>Allamanda cathartica</i>	Apocynaceae	Flower Extract	Aqueous	H ₂ SO ₄ vs NaOH CH ₃ COOH vs KOH	0.1 M	Brown Brown	Yellow Yellow	At P ^H 5.35
Four o'clock ^[41]	<i>Mirabilis jalapa</i>	Nyctaginaceae	Flower extract	Methanolic hydrochloric acid	H ₂ SO ₄ vs NaOH CH ₃ COOH vs KOH	0.1 M 0.5 M 1.0 M	Golden brown Golden brown	Yellow Yellow	At P ^H 5.45
Lantana ^[42]	<i>Lantana camara</i>	Verbenaceae	Flower extract	Ethanollic	HCl vs NaOH HCl vs NH ₄ OH CH ₃ COOH vs NaOH CH ₃ COOH vs NH ₄ OH	1.0 M 0.5 M 0.1 M	Yellow Yellow Yellow Yellow	Colourless Colourless Colourless Colourless	NR NR NR NR
Tropic Flame ^[42]	<i>Crossandra funduliformis</i>	Acanthaceae	Flower extract	Ethanollic	HCl vs NaOH HCl vs NH ₄ OH CH ₃ COOH vs NaOH CH ₃ COOH vs NH ₄ OH	1.0 M 0.5 M 0.1 M	Yellow Yellow Yellow Yellow	Colourless Colourless Colourless Colourless	NR NR NR NR
Marigold ^[42]	<i>Tagetes erecta</i>	Asteraceae	Flower extract	Ethanollic	HCl vs NaOH HCl vs NH ₄ OH CH ₃ COOH vs NaOH CH ₃ COOH vs NH ₄ OH	1.0 M 0.5 M 0.1 M	Yellow Yellow Pink Pink	Colourless Colourless Colourless Colourless	NR NR NR NR
Rose of Sharon ^[42]	<i>Hibiscus syriacus</i>	Malvaceae	Flower extract	Ethanollic	HCl vs NaOH HCl vs NH ₄ OH CH ₃ COOH vs NaOH CH ₃ COOH vs NH ₄ OH	1.0 M 0.5 M 0.1 M	Yellow Light green Pink Pink	Colourless Yellow Colourless Yellow	NR NR NR NR

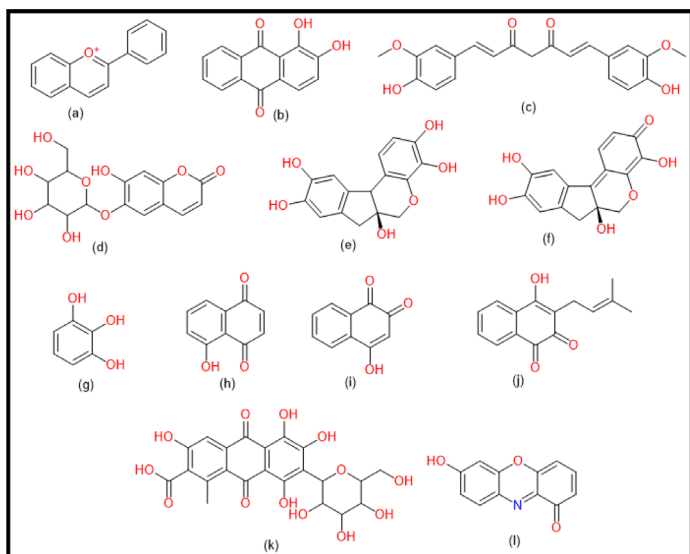


Figure 1: Chemical Structures of Natural Indicators.

contain anthocyanin molecules. Anthocyanin is found in blue flowers including cornflower, blue chicory, and blue rosemary, as well as purple flowers like purple mint, purple passionflower, purple sage, common violet, and lavender. Apart from flowers, anthocyanin can be found in fruits such as apples. *Tradescantia pallida* leaves contain rich sources of anthocyanin, which are used for the prevention of diseases.^[49,51] Numerous anthocyanins from plants revealed different absorption spectra in the range between 465-550 nm,^[35,51] and due to presence of these anthocyanins it produces different colours like red, pink, blue, purple, violet, and orange. Only a few aglycone anthocyanidins are much smaller (about 17).^[52] Six of the 17 anthocyanidins found in nature are cyanidin, delphinidin, pelargonidin, pelargonidin, malvidin, peonidin, and petunidin.^[53] The chemical structures of the above six anthocyanidins were depicted in Figure 3.

Anthocyanidins are divided into three categories: 3-hydroxyanthocyanidins, 3-deoxyanthocyanidins, and O-methylated anthocyanidins, whereas anthocyanins are divided into two categories: anthocyanidin glycosides and acylated anthocyanins. Anthocyanins and their aglycone derivatives (anthocyanidins- malvidin, cyanidin, peonidin, and delphinidin) are flavonoids found in berries (blueberries, bilberries, cranberries, elderberries, raspberry seeds, and strawberries).^[54] There are four types of acylated anthocyanin: acylated anthocyanin, coumaroylated anthocyanin, caffeoylated anthocyanin, and malonylated anthocyanin. The anthocyanidin pigments are amphoteric in nature, and their acid salts are usually red, basic salts provide green, metal salts provide blue and in neutral solution anthocyanidins are violet colour in nature.^[55]

Cyanidin

Cyanidin (Figure 3a) is an anthocyanidin-like natural plant pigment found in berries such as grapes, bilberry, blackberry,

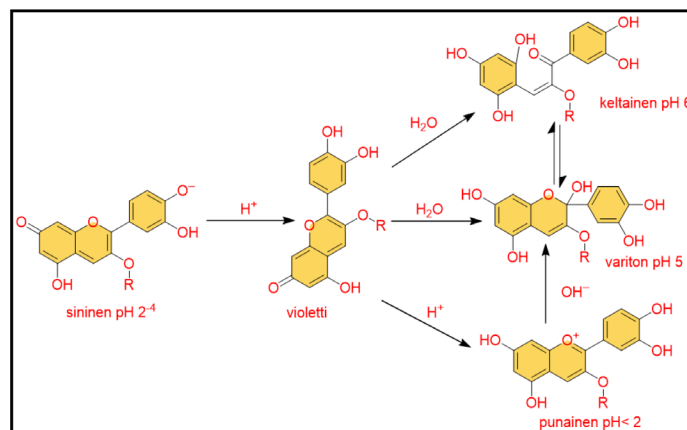


Figure 2: Effect of changes in Anthocyanin structure based on the pH of the surrounding solution.

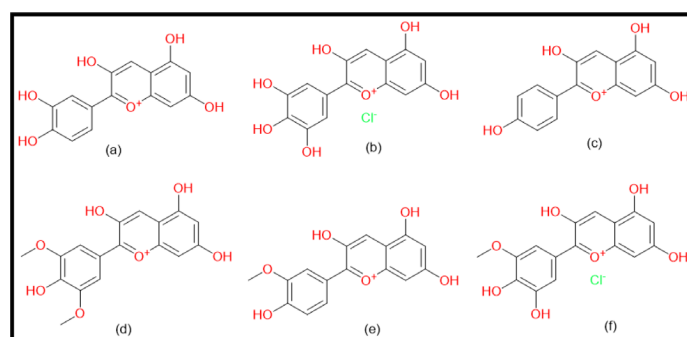


Figure 3: Chemical Structures of different anthocyanin.

blueberry, cherry, cranberry, elderberry, hawthorn, loganberry, açai berry, raspberry, and other red-colored vegetables like red sweet potato, purple corn, red cabbage, and red onion.^[56,57] Other fruits that contain cyanidin include apples and plums. The colour of this natural chemical is a distinctive reddish-purple. The cyanidin molecule has a red colour when pH is less than 3, a violet colour when pH is between 7-8, and a blue colour when pH is greater than 11. The highest concentrations of cyanidin can be found in the seeds and skin of some fruits.

Delphinidin

Delphinidin (Figure 3b) is a natural plant pigment that shows in the plant as a blue-reddish or purple colour.^[58] Delphinidin is the blue pigment found in the flowers of the *Viola* and *Delphinium* genera. Apart from that, delphinidin, which may be found in cranberries, concord grapes, pomegranates, and bilberries, is responsible for the grape's blue-red colour.^[59,60]

Pelargonidin

Pelargonidin (Figure 3c) is mainly a red-coloured pigment, but it provides an orange colour for a few flowers and red colour in some fruits and berries.^[61-63] Pelargonidin can be found in red geraniums, spathes of philodendron Pelargonidin is found in mature raspberries, strawberries, blueberries, blackberries,

cranberries, saskatoon berries, and chokeberries, among other berries.^[64] The red radishes colour of pelargonidin is found in plums and pomegranates.^[65] It is also present in higher content in kidney beans.^[66]

Malvidin

Malvidin (Figure 3d) is a glycosylated anthocyanidin with the sugar moiety connected at position 3 on the c-ring, resulting in malvidin-3-glucoside and malvidin-3-galactoside.^[67] Malvidin is found in the blue petal of the polyanthus group's primula (*Anagallis monelli*). Malvidin is also responsible for red wine's colour.^[68] Blueberries (*Vaccinium corymbosum*) and saskatoon berries (*Amelanchier alnifolia*) also contain it.^[69,70] Malvidin solutions that are slightly acidic and neutral are red, while basic malvidin solutions are blue.

Peonidin

Peonidin is an O-methylated anthocyanidin derived from cyanidin (Figure 3e). Some flowers, such as peonies and roses, have a purplish-red colour due to peonidin. Some blue flowers, such as the morning glory, contain peonidin. At pH 2, peonidin is cherry red; at pH 3, it is a strong yellowish pink colour; at pH 5, a red-purple grape colour; and at pH 8 it becomes deep blue colour. It is stable at higher pH and has been isolated as a blue colourant from the brilliant "Heavenly Blue" morning glory (*Ipomoea tricolor*).^[71]

Petunidin

Petunidin (Figure 3f) is a dark-red or purple water-soluble pigment found in many red berries, including choke berries (*Aronia* sp.), saskatoon berries (*Amelanchier alnifolia*), and other grape species. It's also responsible for the colours of many flowers' petals. When the fruits are exposed to sunshine, it produces the deep purple colour of indigo rose tomatoes.^[72] The molecule's name is derived from the word Petunia.

Alizarin

Alizarin (Figure 1b) is an orange dye that is present in the form of a glycoside in the root of the madder plant, *Rubia cordifolia* L., *Oldenlandia umbellata* L. (Indian Madder), *Rubia tinctorum* L. (European Madder).^[8,73] At pH 5.5 in 0.5%, the alcoholic solution of alizarin provides a yellow colour, and at pH 6.8, it appears to be in red.^[8]

Curcumin

Curcumin (Figure 1c) is a yellow pigment derived from the *Curcuma longa* (turmeric) plant.^[74] Turmeric contains 2 percent to 9 percent curcuminoids, depending on its origin and soil characteristics. Curcumin, demethoxycurcumin, bis-demethoxycurcumin, and cyclic curcumin are examples of curcuminoid chemicals. Curcumin is the primary component, while cyclic curcumin is the secondary component. Curcumin

is primarily a symmetric molecule called diferuloylmethane. The colour of curcumin changes from yellow to red when the pH is between 7.5 and 8.5. At 467 nm, the curcumin is entirely deprotonated (red) under an alkaline pH (>pH 10).^[75]

Esculin

The esculin (7-hydroxycoumarin-6-glucoside) is a fluorescent dye obtained from *Aesculus* spp., including *A. glabra*, *A. californica*, *A. octandra*, *A. pavia* and *A. hippocastanum*.^[76] Esculin changes the colourless to fluorescent blue at pH 1.5 – 2.^[8] The chemical structure of esculin was depicted in Figure 1d.

Logwood

Logwood is a dye present in the yellow heartwood of *Haematoxylon campechianum*. The dyestuff contains the substance haematoxylin, but when exposed to air, it is oxidized and produce the purple compound hametoxylin (Figure 1e) or haematein (Figure 1f). In an acidic medium, the colour logwood produce reddish colour, and in the alkaline medium, it produces blue shades.^[77]

Pyrogallol

Pyrogallol (Figure 1g) is derived from the aquatic plant *Myriophyllum spicatum*. Pyrogallol gives colourless to golden yellow in the variation of pH range 7.4 - 10.0.^[78]

Juglone and Lawsone

The chemicals juglone [5-hydroxy-1, 4-naphthoquinone] and lawsone [2-hydroxy-1, 4-naphthoquinone] were isolated from Juglandaceae and Lythraceae plants, respectively. In an acidic media, juglone (Figure 1h) and lawsone (Figure 1i) have minor pale-yellow colours. But in the alkaline medium, they reveal pink and red colours.^[79]

Lapachol

Plants in the Bignoniaceae and Verbenaceae families produce lapachol [2-hydroxy-3-(2-methyl-3-butenyl)-1, 4-naphthoquinone]. The compound is present mainly in the heartwood of *Tecomella undulate*, *Tabebuia rosea*, and *Phyllarthron comorensis*.^[80] The lapachol (Figure 1j) is also present in the stem bark of *Stereospermum suaveolens*.^[81] Because protonation of the quinonoid oxygen atom suppresses its quinonoid character, it produces colourless acidic media. However, because of its resonant structures, it has a red colour in the alkaline medium. Lapachol transition range is found to be in between the pH range of 4.8-5.8.^[80]

Cochineal

Cochineal (Figure 1k) is an acid-base indicator obtained from the bodies of dried female insects *Dactylopius coccus* Costa. Cochineal extract is obtained by using an aqueous-alcoholic or by alcoholic solution. But now a day's cochineal solutions are not used as indicators in acid-base titration.^[82,8]

Litmus

Litmus (Figure 11) is a dye derived from lichens of diverse types. Litmus is most commonly used to determine if a solution is acidic or basic. When exposed to acidic conditions, blue litmus paper turns red, and when exposed to alkaline conditions, red litmus paper turns blue. Purple is the colour of neutral litmus paper.^[8,83]

Easter egg dyes

Easter egg decorating with a natural pH indicator that is also a natural Easter egg dye, for example, purple beetroot, cabbage, and yellow turmeric are used as natural pH indicator egg dye. The blue or purple colour from the cabbage mixed with the yellow-orange colour of the turmeric dye or Easter eggs green. Because the Easter egg dye is a natural pH sensor, it will change colour if a strong acid or strong base is present. The colour of the easter egg varies depending on the ingredients (lemon juice vs. citric acid) and the natural Easter egg dye utilised (beets versus cabbage versus turmeric, etc.). The colour of eggshells changed from green to yellow when to be painted on lemon juice, an acid.^[84] The potential of a natural indicator as for example extract of *Areca catechu* seed when assessed in comparison to a synthetic indicator like phenolphthalein was found to be similar. Comparison of end points in four different acid-base titrations helped in better understanding. The acid-base titrations such as strong acid-strong base (HCl v/s NaOH), weak acid-strong base (CH₃COOH v/s NaOH), strong acid-weak base (HCl v/s NH₄OH), and weak acid-weak base (CH₃COOH v/s NH₄OH) were performed using both of the indicators to compare accuracy. In strong acid-strong base system it was found that the extract of *Areca Catechu* seed yields an end-point of 5 mL of titrant quantity while phenolphthalein gives an end point of 4.8 mL. For strong acid-weak base system *Areca catechu* shows an end-point at 3.7 mL while that of phenolphthalein is 4.4 mL. In case of weak acid-strong base type, *Areca catechu* seed extract gives an end-point at 5.4 mL of titrant volume whereas phenolphthalein gives the end-point at 5.1 mL. In the weak acid-weak base system, *Areca catechu* seed extract yields end-point at 4 mL just similar to that of phenolphthalein, which shows an exact end point at 4 mL of titrant volume. In all these titrations performed the *Areca catechu* seed extract provides a colour change from yellowish to reddish that marked the end-points. These data's show that the seed extract of *Areca catechu* gives close endpoint result when compared with the synthetic indicator like phenolphthalein. Also, it confirms that the seed extract of *Areca catechu* acts as quite an accurate tool as a universal green indicator.^[85]

CONCLUSION

The review reflects many natural-based indicators like curcumin, lapachol, cochineal, juglone, lawsone and many other phytochemicals may have effective indicator properties. Due to molecular structure, functionality of phytochemicals, they act as

an indicator. These pigments and phytoconstituents were isolated by different extraction methods by the application of various solvents, and as an indicator, they possess sharp colour changes at different pH levels in acid-base titrations. So, considering advantages like eco-friendly, simplicity, non-hazardousness properties, these natural-based indicators were preferred against synthetic ones. Literature survey reveals, a limited number of phytoconstituents and pigments. So, the demand for new natural pigments is needed for experimental studies with accurate and sharp results.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ABBREVIATIONS

M: Molarity; **N:** Normality; **NR:** Not Reported; **FDA:** Food Drug and Administration.

REFERENCES

- Izonfuo W, Fekarurhobo G, Obomanu F, Daworiye L. J Appl Sci Environ Manag. 2006;10:5.
- Pharmaceutical analysis. A.V. Kature, K.R. Mahadik. Nirali Prakashan. 17th ed. 2012;6.
- Gupta P, Jain P, Jain PK. Dahalia flower sap a natural resource as indicator in acidimetry and alkalimetry. Int J Pharm Tech. 2012. 4(4):5038-5045.
- Kature AV, Mahadik KR, Wadodkar SG, More HN. A textbook of pharmaceutical analysis. 11th ed. Vol. 1. Maharashtra, India: Nirali Prakashan; 2005.
- Mendham J, Denney RC, Barnes JD. Quantitative chemical analysis. 6th ed. New Delhi, India: W H Freeman; 2004.
- Pimpodkar NV, Shikalgar S, Shinde N, Bhise S, Surve B. Asian J Pharm Anal Chem. 2014;4:82.
- Pimpodkar NV, Surve BS, Bhise SH. Use of *Argyria cuneata* flowers extract as a natural indicator in acid base titration. J Curr Pharma Research. 2014. 4(4): 1124-1127.
- Vankar PS, Bajpai D. Rose anthocyanins as acid base indicators. EJEAFCh. 2010. 9(5):875-884.
- Burungale SH, Mali AV. Natural indicator as an eco-friendly in acid base titration. J Chem Pharm Res. 2014. 6:901-903.
- Pradeep DJ, Dave K. A novel, inexpensive and less hazardous acid-base indicator. J Lab Chem Educ. 2013. 1:34-38.
- Bhuvaneswari B, Sivaelango G, Parthiban D, Arun N, Kumaravel P. Natural dyes as acid-base indicators from *Beta vulgaris*. Research J Pharmacogn Phytochem. 2015. 7(2) Suppl1:65-68.
- Jaspreet S, Kanika A, Perminder N, Geeta D. Herbal indicators as an upcoming trend in titrimetric analysis. Int Res J Pharm. 2011. 2(4):177-179.
- Kadam S, Yadav A, Raje V, Waghmare K. Comparative study of natural and synthetic indicators. Der Pharma Chemica. 2013. 5(1):296-299.
- Pathade KS, Patil SB, Konda-War MS, Naik-Wade NS, Magdum CS. Int J Chem Technol Res. 2009;1:549.
- Abugri DA, Apea OB, Pritchett G. Investigation of a Simple and Cheap Source of a Natural Indicator for Acid-Base Titration: Effects of System Conditions on Natural Indicators. Green Sustain Chem. 2012;02(3):117-22. doi: 10.4236/gsc.2012.23017.
- [cited Aug 11 2019] Available from: http://en.wikipedia.org/wiki/ph_indicator. Wikipedia.
- [cited Aug 12 2019] Available from: <http://www.ch.ic.ac.uk/vchemlib/course/indi/indicator.html>.
- Bahadori A, Maroufi NG. Volumetric acid-base titration by using of natural indicators and effects of solvent and temperature. Austin Chromatogr. 2016. 3(1):1-4.
- [cited Aug 22 2019] Available from: <https://www.westlab.com/blog/2017/11/15/how-does-temperature-affect-ph>.

20. <https://www.sylvania.com/en-us/innovation/education/light-andcolor/Pages/relationships-between-color-and-light.aspx>. [accessed Sep 14 2019].
21. Sidana J, Kanika A, Parminder N, Geeta D. *Int Res J Pharm*. 2011;2:177.
22. Patrakar R, Deshpande A, Walsangikar S, Niranjane K, Gadgul A. *Pharm Lett*. 2010;2:520.
23. Vyas AD, Biren S, Modi N, Dikhit C, Vijay L. *Int J PharmSci*. 2012;3:2211.
24. Wadkar KA, Magdum CS, Kondawar MS. *Res J Pharm Technol*. 2008;1:535.
25. Gupta P, Jain P, Jain PK. *Int J Pharm Technol*. 2013;4:5038.
26. Patil SB, Kondawar MS, Ghodke DS, Naikwade NS, Magdum CS. *Res J Pharm Technol*. 2009;2:421.
27. Gupta P, Jain P, Jain PK. *Int J Pharm Technol*. 2012;4:1619.
28. Abbas SK. Study of acid-base indicator property of flowers of *Ipomoea biloba*. *Int Curr Pharm J*. 2012;1(12):420-2. doi: 10.3329/icpj.v1i12.12452.
29. Deshpande A, Jadge D, Dhawale S, Patrakar R, A Gadgul. *J Pharm Res*. 2010;3:2512.
30. Patrakar R, Gond N, Jadge D. *Int J PharmTech Res*. 2010;2:1954.
31. Pathade KS, Patil SB, Kondawar MS, Naikwade NS, Magdum CS. *Int J ChemTech Res*. 2009;1:549.
32. Patil MV, Jadhav RL. *Int J Pharm Pharm Sci*. 2012;4:490.
33. Agrawal S, Raj NR, Chouhan K, Raj CN, Jain S, Balasubramaniam A. *J Chem Pharm Res*. 2011;3:168.
34. Bhuvaneshwari B, Sivaelango G, Parthiban D, Arun N, P Kumaravel. *J Pharmacogn Phytochem*. 2015;7:65.
35. Zulfajri M, Muttakin. Activity analysis of anthocyanin from *Syzygium cumini* (L.) skeels as a natural indicator in acid-base titration. *Rasayan J Chem*. 2018. 11(1):135-141.
36. Patrakar R, Gond N, Jadge D. Flower extract of *Jacaranda acutifolia* used as a natural indicator in acid base titration. *Int J Pharmtech Res*. 2010. 2(3):1954-1957.
37. Abbas SK. A study on pH indicator property of flowers of *Ipomea nil*. *J Innov Pharm Biol Sci*. 2014. 1(2) 72-76.
38. Okoduwa SI, Mboral LO, Adu ME, Adeyi AA. Comparative Analysis of the Properties of Acid-Base Indicator of Rose (*Rosa setigera*), Allamanda (*Allamanda cathartica*), and Hibiscus (*Hibiscus rosa-sinensis*) Flowers. *Biochem Res Int*. 2015;2015:381721. doi: 10.1155/2015/381721, PMID 26819757.
39. Kapilraj N, Keerthanan S, Sithambaresan M. Natural plant extracts as acid-base indicator and determination of their pKa value. *J chem*. 2019. 1-6.
40. Garba MD, Abubakar S. Flower extract as an improvised indicator in acid-base titration. *Chemsearch J*. 2012. 3(1):17-18.
41. Shishir MN, Laxman JR, Vinayak PN, Jacky DR, Bhimrao GS. Use of *Mirabilis jalapa* L. flower extract as a natural indicator in acid base titration. *J Pharm Res*. 2008;1(2):159-162.
42. Thorat MB, Pawar PR, Shelar PA. Natural Indicators. *J Curr Pharm Res*. 2014;4(4):1336-42.
43. Laleh GH, Frydoonfar H, Heidary R. The effect of light, temperature, pH and species on stability of anthocyanin pigments in four Berberis species. *Pak J Nutr*. 2006. 1:90-92.
44. Kong J, Chia LS, Goh NK, Chia TF. Analysis and biological activities of anthocyanins. *Phytochem*. 2008. 64(5): 923-933.
45. Rymbai H, Sharma RR, Srivastav, M. Biocolorants and its implications in Health and Food Industry - A Review. *Int. J. PharmTech Res*. 2011. 3(4):2228-2245.
46. Brouillard R, Dangles O. Anthocyanin molecular interactions: the first step in the formation of new pigments during wine aging? *Food Chem*. 1994;51(4):365-71. doi: 10.1016/0308-8146(94)90187-2.
47. Jackman RL, Smith JL. Anthocyanins and betalains. In: Hendry GAF, et al., editors. *Natural food colorants*. Springer; 1996:182-241.
48. Wahyuningsih S, Wulandari L, Wartono MW, Munawaroh H, Ramelan AH. *Int Conf Food Sci Eng*. 2017: 4;1.
49. He K, Li X, Chen X, Ye X, Huang J, Jin Y, et al. Evaluation of antidiabetic potential of selected traditional Chinese medicines in STZ-induced diabetic mice. *J Ethnopharmacol*. 2011;137(3):1135-42. doi: 10.1016/j.jep.2011.07.033, PMID 21798327.
50. He F, Mu L, Yan GL, Liang NN, Pan QH, Wang J, et al. Biosynthesis of anthocyanins and their regulation in colored grapes. *Molecules*. 2010;15(12):9057-91. doi: 10.3390/molecules15129057, PMID 21150825.
51. Mónica GM, Wrolstad RE. Characterization and Measurement of Anthocyanins by UV-Visible Spectroscopy. *Curr Protocols Food Anal Chem*. 2001. F:1.2.1-1.2.13.
52. Harborne JB, Grayer JN. The anthocyanins In: Harborne although the Hemical structure of *Anthocyanins*. The flavonoids: Advances in Research since 1980. Chapman and Hall. London. 1988. 1-20.
53. Francis FJ. Food colorants: anthocyanins. *Crit Rev Food Sci Nutr*. 1989;28(4):273-314. doi: 10.1080/10408398909527503, PMID 2690857.
54. Mecocci P, Tinarelli C, Schulz RJ, Polidori MC. Nutraceuticals in cognitive impairment and Alzheimer's disease. *Front Pharmacol*. 2014;5:147. doi: 10.3389/fphar.2014.00147, PMID 25002849.
55. Finar IL. Stereochemistry and chemistry of natural products. *Organic chemistry*. 5th ed. Vols. 769-770. Edinburgh Gate, Harlow, Essex: Addison Wesley Longman Limited; 1975. p. CM202JE, England. 2.
56. [cited Nov 9 2019] Available from: <http://www.phytochemicals.info/phytochemicals/cyanidin.php>.
57. Cevallos-Casals BA, Cisneros-Zevallos L. Stoichiometric and kinetic studies of phenolic antioxidants from Andean purple corn and red-fleshed sweetpotato. *J Agric Food Chem*. 2003;51(11):3313-9. doi: 10.1021/jf034109c, PMID 12744660.
58. Katsumoto Y, Fukuchi-Mizutani M, Fukui Y, Brugliera F, Holton TA, Karan M, et al. Engineering of the rose flavonoid biosynthetic pathway successfully generated blue-hued flowers accumulating delphinidin. *Plant Cell Physiol*. 2007;48(11):1589-600. doi: 10.1093/pcp/pcm131, PMID 17925311.
59. Ribéreau-Gayon J, Ribéreau-Gayon P. *Am J Enol Vitic*. 1958;9:9.
60. Lähti AK, Riihinen KR, Kainulainen PS. Analysis of anthocyanin variation in wild populations of bilberry (*Vaccinium myrtillus* L.) in Finland. *J Agric Food Chem*. 2008;56(1):190-6. doi: 10.1021/jf072857m, PMID 18072741.
61. Bąkowska-Barczak A. Acylated anthocyanins as stable, natural food colorants - A review. *Pol J Food Nutr Sci*. 2005. 14/55(2):107-116.
62. Robinson GM, Robinson R. A survey of anthocyanins.II. *Biochemical J*. 1932;6(5):1647-1663.
63. Jaakola L. New insights into the regulation of anthocyanin biosynthesis in fruits. *Trends Plant Sci*. 2013. 18(9):477-483.
64. Mazza G. Compositional and Functional Properties of Saskatoon Berry and Blueberry. *Int J Fruit Sci*. 2005;5(3):101-20. doi: 10.1300/J492v05n03_10.
65. Nishio T, Kitashiba H. *The radish genome*. 1st ed. New York: Springer; 2017.
66. Lin LZ, Harnly JM, Pastor-Corrales MS, Luthria DL. The polyphenolic profiles of common bean (*Phaseolus vulgaris* L.). *Food Chem*. 2008;107(1):399-410. doi: 10.1016/j.foodchem.2007.08.038, PMID 25544796.
67. Huang W, Zhu Y, Li C, Sui Z, Min W. Effect of blueberry anthocyanins malvidin and glycosides on the antioxidant properties in endothelial cells. *Oxid Med Cell Longev*. 2016. 1-10.
68. *Phytochemicals: malvidin*. Top Cultures.
69. Mazza G. Compositional and functional properties of saskatoon berry and blueberry. *Int J Fruit Sci*. 2005. 5(3):99-118.
70. Bakowska-Barczak AM, Marianchuk M, Kolodziejczyk P. Survey of bioactive components in Western Canadian berries. This article is one of a selection of papers published in this special issue (part 2 of 2) on the Safety and Efficacy of Natural Health Products. *Can J Physiol Pharmacol*. 2007;85(11):1139-52. doi: 10.1139/Y07-102.
71. [cited Sep 17 2019] Available from: <https://en.wikipedia.org/wiki/Peonidin>. Wikipedia.
72. [cited Aug 20 2019] Available from: http://horticulture.oregonstate.edu/purple_tomato_faqs.
73. Singh HB, Bharati KA. Vol. 33. Woodhead Publishing India Pvt, Ltd., 2014. p. 260.
74. Lestari MLAD, Indrayanto G. Curcumin. *Profiles Drug Subst Excipients Relat Methodol*. 2014:113-204.
75. Priyadarsini KI. The chemistry of curcumin: from extraction to therapeutic agent. *Molecules*. 2014;19(12):20091-112. doi: 10.3390/molecules191220091, PMID 25470276.
76. Keebler CM, Facik F. Cytopreparatory techniques. In: Bibbo M, Wilbur DC, editors. *Comprehensive cytopathology*. Saunders/Elsevier; 2008. p. 977-1003.
77. [cited Oct 12 2019] Available from: <http://sentr.ischool.utexas.edu/~cochineal/pdfs/e-hammeke-04-logwood.pdf>.
78. Pradeep DJ, Dave K, Novel A. Inexpensive and Less Hazardous Acid-Base Indicator. *J Lab Chem Educ*. 2013. 1(2):34-38.
79. Joshi KC, Singh P, Singh G. Juglone and Lawsone as Acid-Base Indicators. *Z Naturforsch*. 1977. 32 b:890-892.
80. Joshi KC, Singh P. Lapachol: A new acid base indicator. *Talanta*, Pergamon Press. 1976. 23:325-326.
81. Nag M, Mukherjee PK, Chanda J, Biswas R, Harwansh RK, NA. Al-Dhabi, V. Duraipandiyani. *Indian J Tradit Know*. 2015;14:590.
82. [cited Sep 4 2019] Available from: http://www.fao.org/fileadmin/user_upload/jecfa_additives/docs/Monograph1/Additive-137.pdf.
83. Neupert M. Lackmus in Römpp Lexikon Chemie (German); January 31, 2013.
84. [cited Sep 15 2019] Available from: <https://rosieresearch.com/natural-dye-color-changing-easter-eggs>.
85. Raghavendra N, Hublikar VL, Chitnis RS, Joseph AR, Sheelmath SD, Pattan SP. *J Water Environ Nanotechnol*. 2020;5:129.

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