Pharmaceutical colourants

Overwiev of approved and used pharmaceutical colourants

A possible classification:
1. Inorganic pigments
2. Organic dyes
2.1 Lipophilic dyes
2.1.1 Carotenoids
2.1.2 Xanthophyls
2.2 Hydrophilic dyes
2.2.1 Fused-rings glycosides, pseudoglycosides and their aglycones
2.2.2 Phenolic dyes not based on fused rings
2.2.3 Indole dyes
2.2.4 Hydrophilic azo-dyes
2.2.5 Hydrophilic triarylmethane dyes

1.Inorganic pigments

•in most insoluble or poorly soluble in both water and organic solvents
•colouring of tablet mass, capsules, surface films on coated tablets
•colouring of suspension creams and oitments

$CaCO_3$, E 170

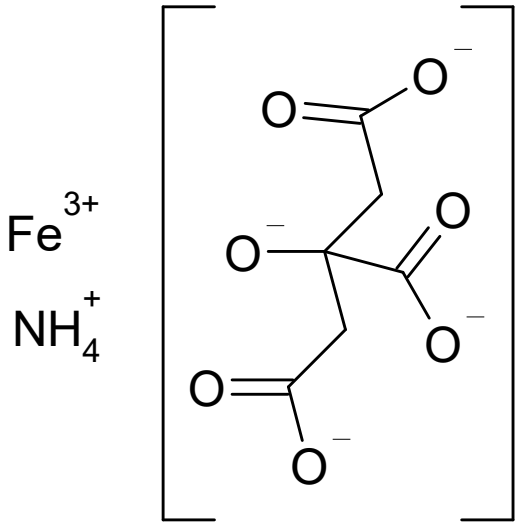
•only for surface „colouring“

TiO_2, E 171, CI 77891, titane white

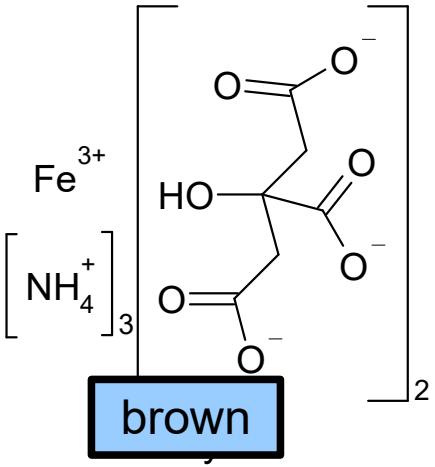
•also protecting factor against UV irradiation

Iron oxides and hydroxides E 172

Ferric-ammonium citrate

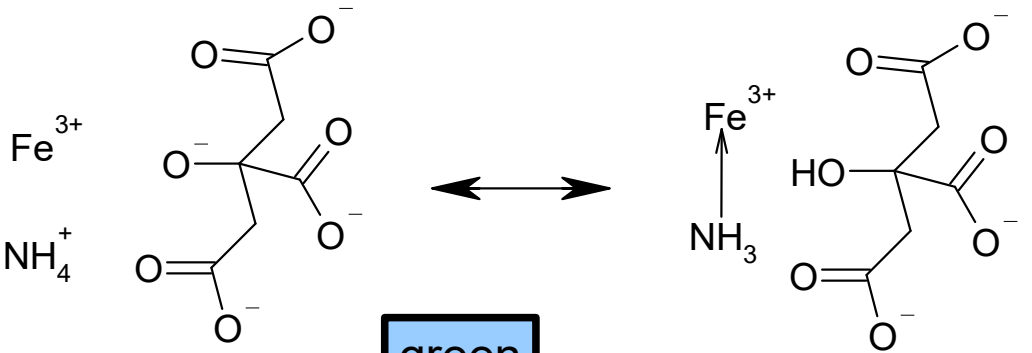


•Steinsvik S. et al.: J. Phys. Chem. Solids 58, 969 (1997)
•water soluble
•since 2002 rejected as a colourant; before 2002 approved in USA; still listed in DAC (=Deutsches Arzneimittel Codex = German Medicines Codex)



brown

21,08 % Fe



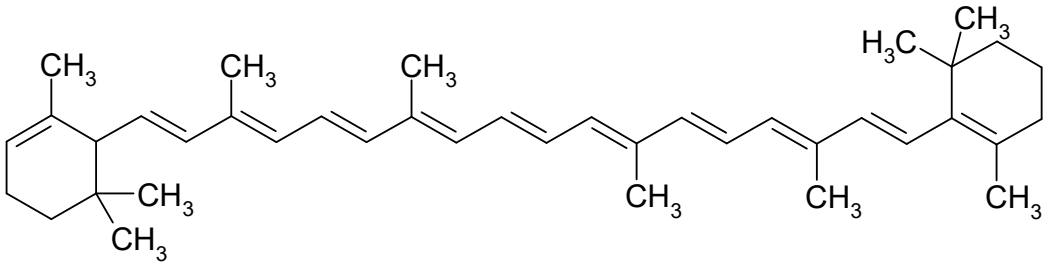
green

11,44 % Fe

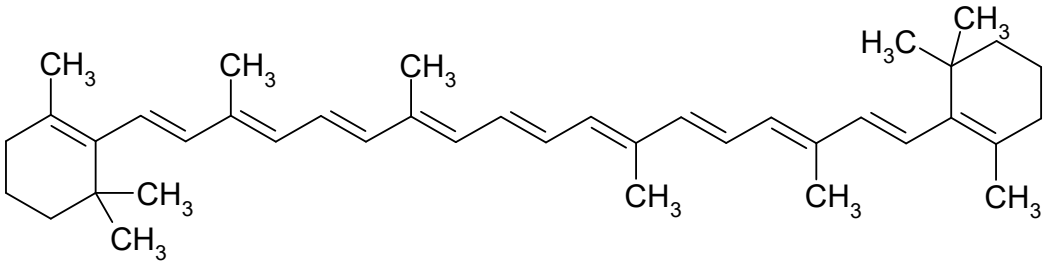
1. Inorganic pigments

Al E 173, CI 77000
•finely powdered - inflammable (pyrophoric)

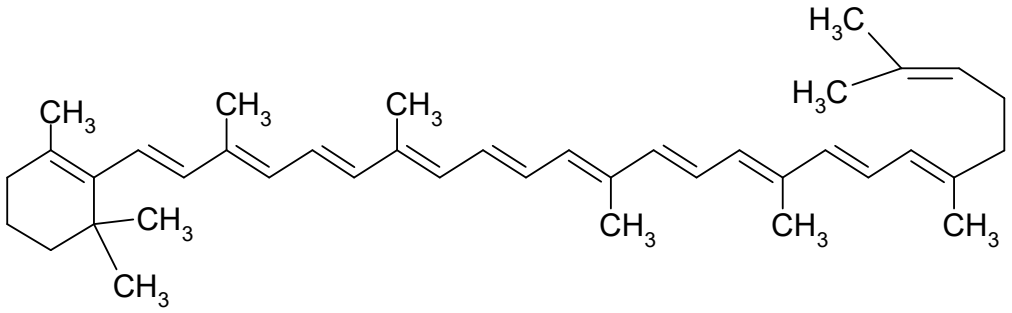
2.1. Lipophilic organic dyes
Carotenoids (together E 160)
α, β, γ-carotene together E 160a



α–carotene (β,ε–carotene)
m.p. 187,5°C
•log $P_{o/w}$ = 17.49

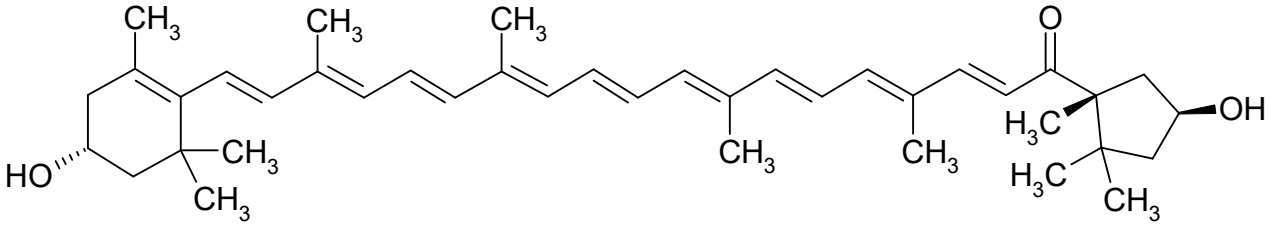


β-carotene
CI 75130 (natural), CI 40800 (syntethtic)
E 160a
m.p. 183°C
•poorly stable on air and light
•from light yellow to deep orange in dependence on concentration
•0.1% for suppositories
•log $P_{o/w}$ = 17.63

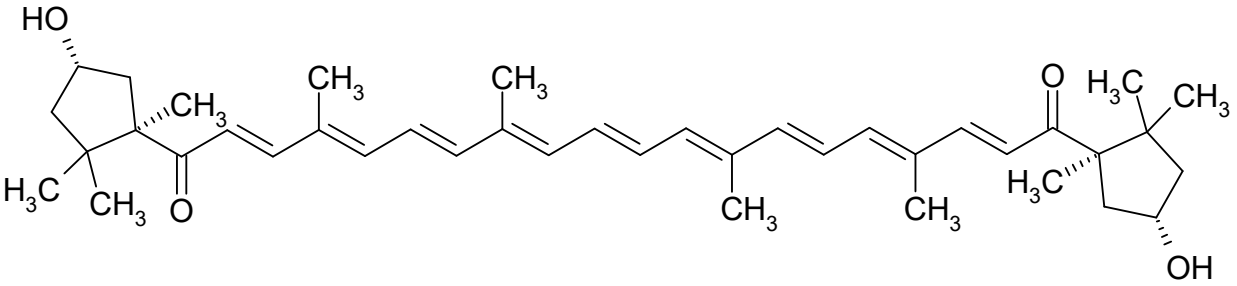


γ-carotene (β,θ–carotene)
m.p. 154°C
•log $P_{o/w}$ = 17.63

Carotenoids (together E 160) - continued

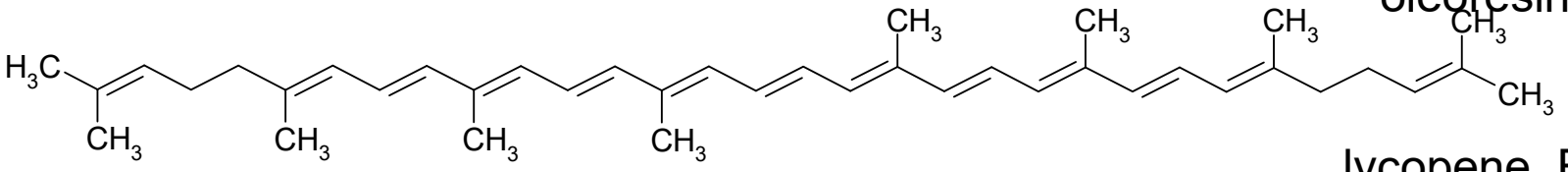


capsanthine, E 160b
•from bell peppers



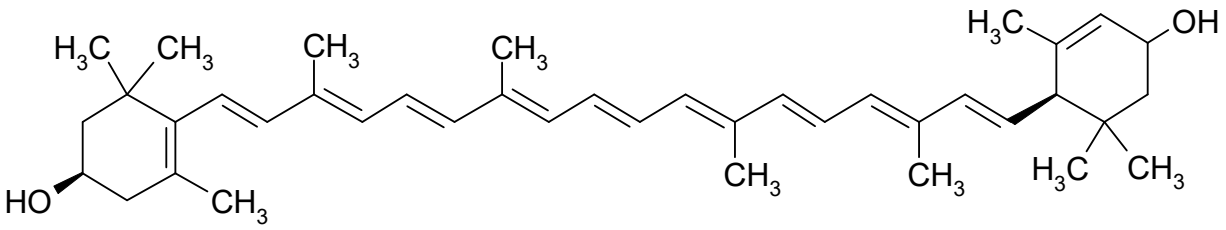
capsorubine, E 160c
•from bell peppers

(capsanthine + capsorubine = bell peppers extract, Paprika oleoresin)

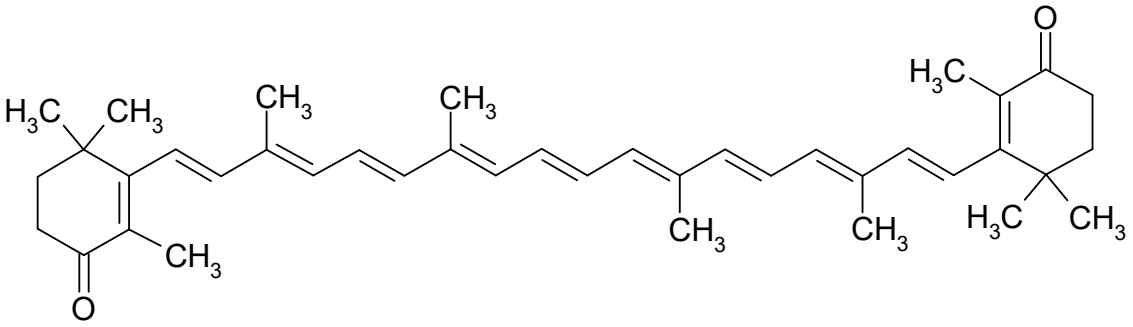


lycopene, E 160d, CI 75125
• from tomatoe
•yellow
•m.p. 175°C
•log $P_{o/w}$ = 17.64

Xanthophyls
•together E 161



luteine, E 161b
•colourant of the egg yolk
•m.p. 196°C
•log $P_{o/w}$=14.82



canthaxanthine, CI 40850, E 161g
•orange
•log $P_{o/w}$=14.1
•antioxidant, believed to be a cancer protectant

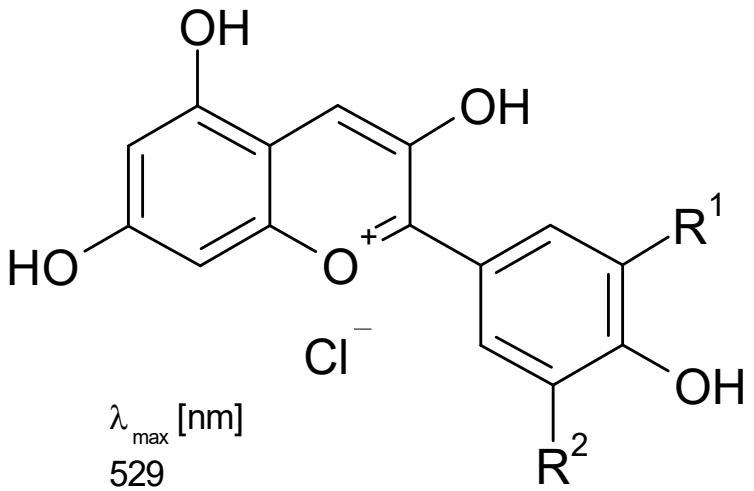
2.1 Hydrophilic organic dyes

2.1.1 Fused-rings glycosides, pseudoglycosides and their aglycones

Anthocyanidines

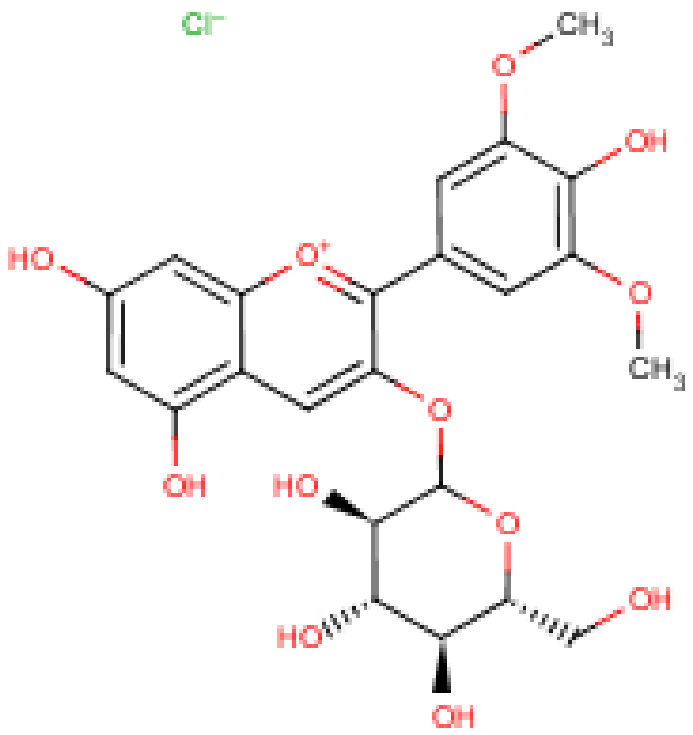
= hydroxylated and methoxylated derivatives of 2-phenylbenzopyrylium

- together E 163
- aglycones of anthocyanins



Name	R^1	R^2	origin	m.p. [°C]	log $P_{o/w}$	colour	λ_{max} [nm]
pelargonidine	H	H	*Pelargonium*	> 350	2.68	salmon	529
kyanidin	OH	H	*Cyanus*	> 300	2.2	red	544
delphinidine	OH	OH	*Delfinium*	> 350	2.14	blue	553
peonidine	OCH_3	H	*Peaeonia*			red	543
petunidine	OCH_3	OH	*Petunia*			blue-red	522
malvidine	OCH_3	OCH_3	*Malva*	> 300; 202-203	2.33	pink-red	553

- in plants as glycosides in most in position 3, particularly esterified with subst. cinnamic acids or acetic acid in pos. 6
- the colour of free aglycons depends on pH: blue in alkaline, red in acidic, this is not valid for glycosides
- increasing number of hydroxyles results in a more intense colour, methylation of hydroxyles shifts the shade from blue to red



malvidine-3-glucoside

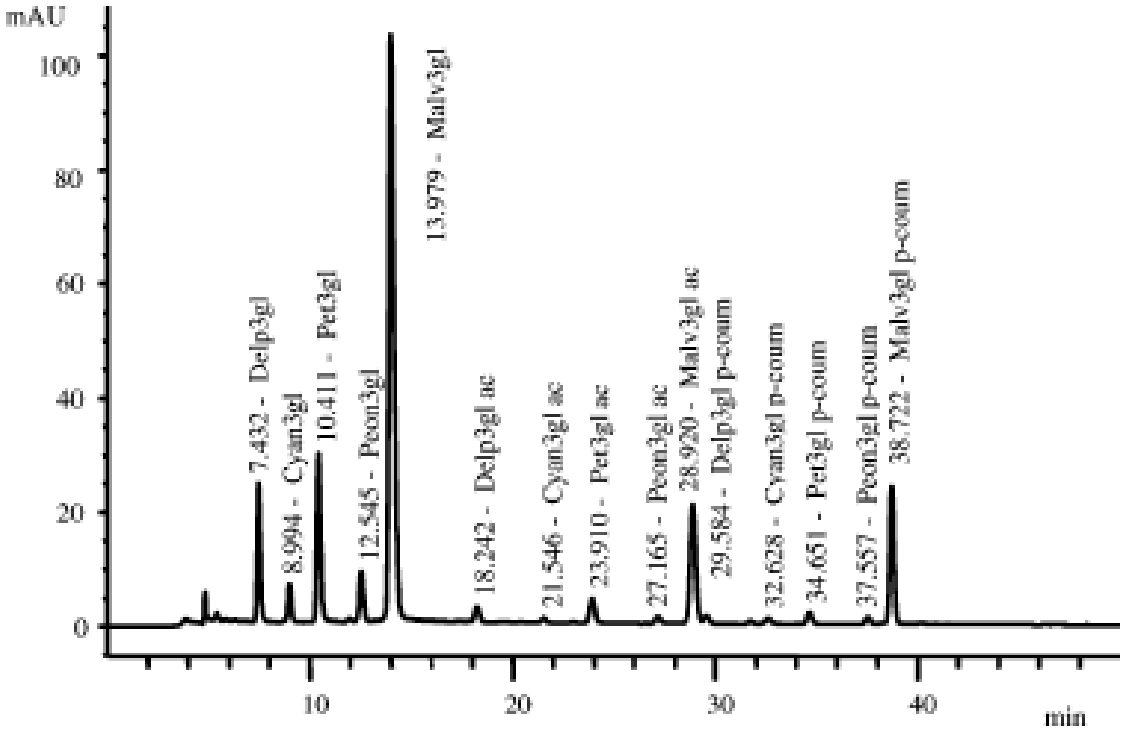
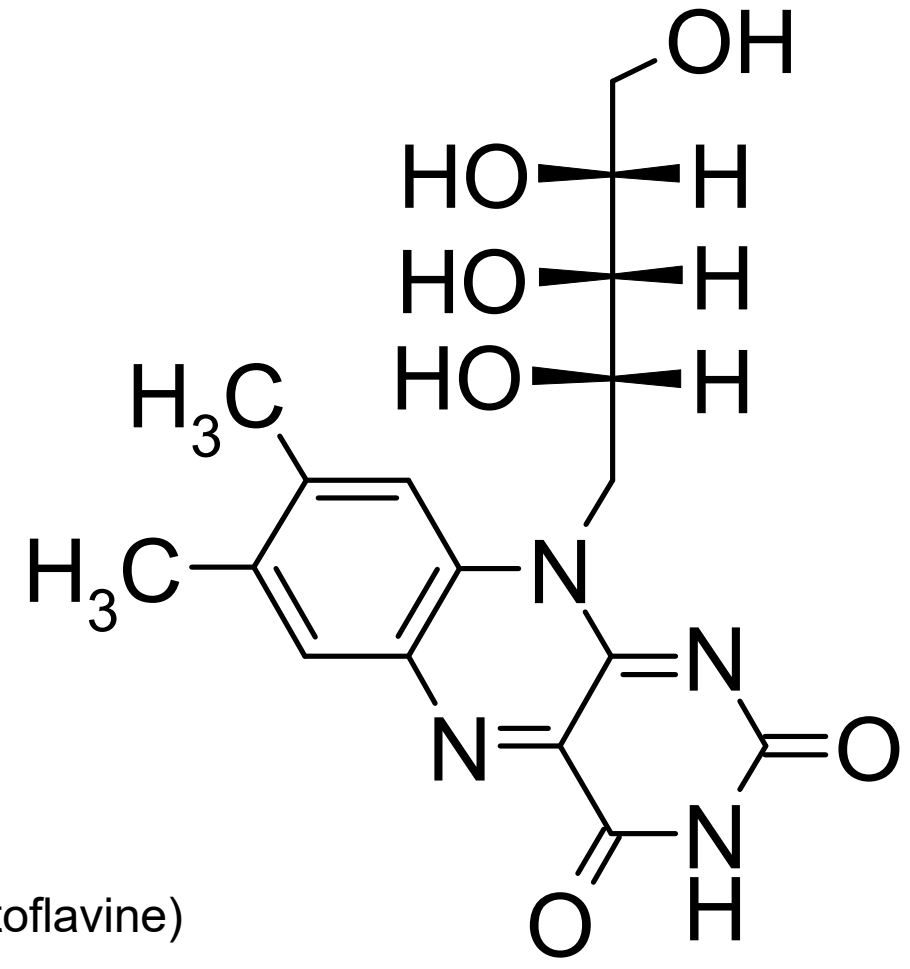
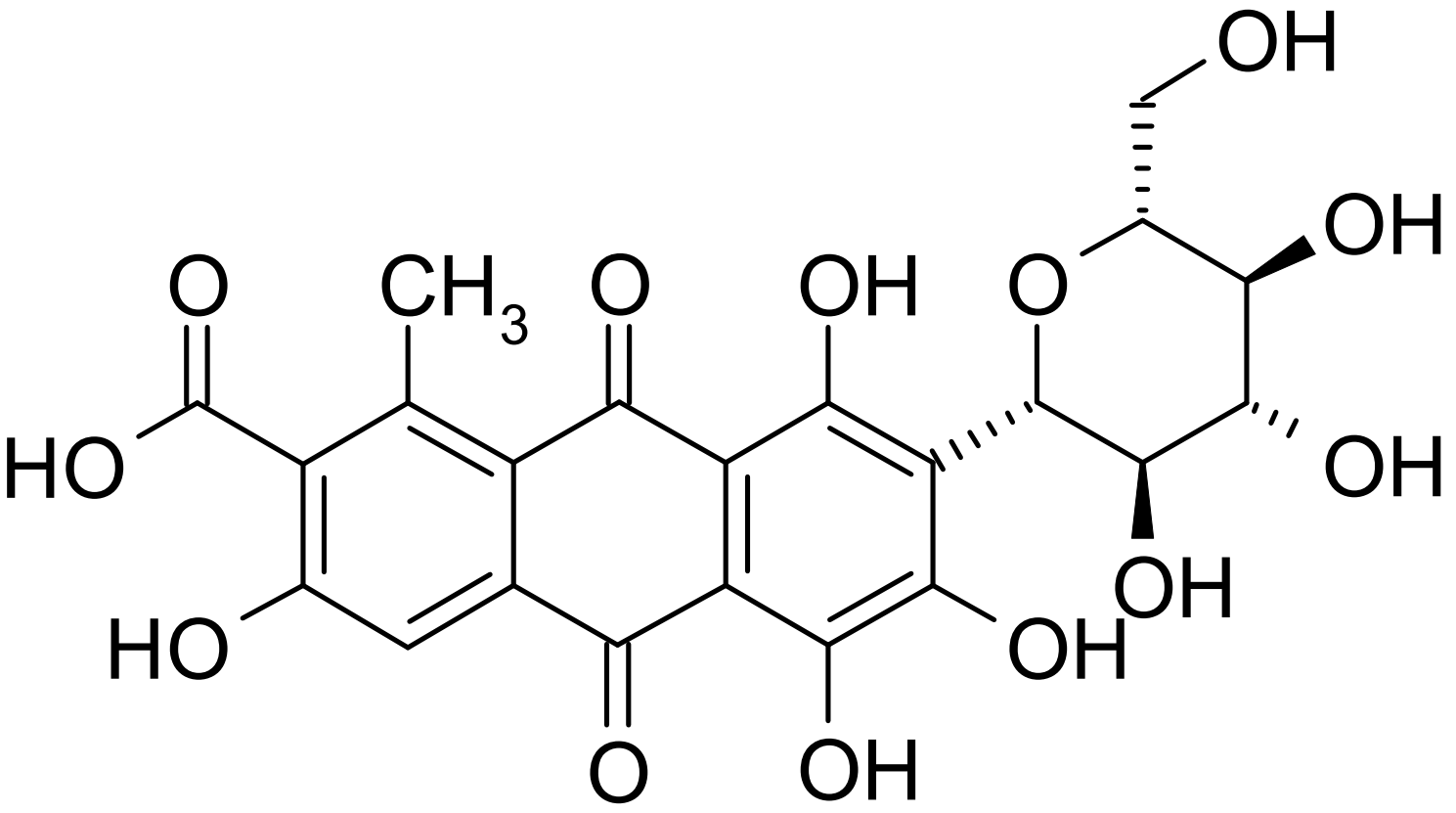


Figure 1. Representative profile of a grape extract analyzed by reversed phase HPLC at 520 nm, as described under Materials and Methods: delphinidin 3-glucoside (Delp3gl), cyanidin 3-glucoside (Cyan3gl), petunidin 3-glucoside (Pet3gl), peonidin 3-glucoside (Peon3gl), malvidin 3-glucoside (Malv3gl), and their corresponding acetic acid (ac) and *p*-coumaric acid esters (p-coum).



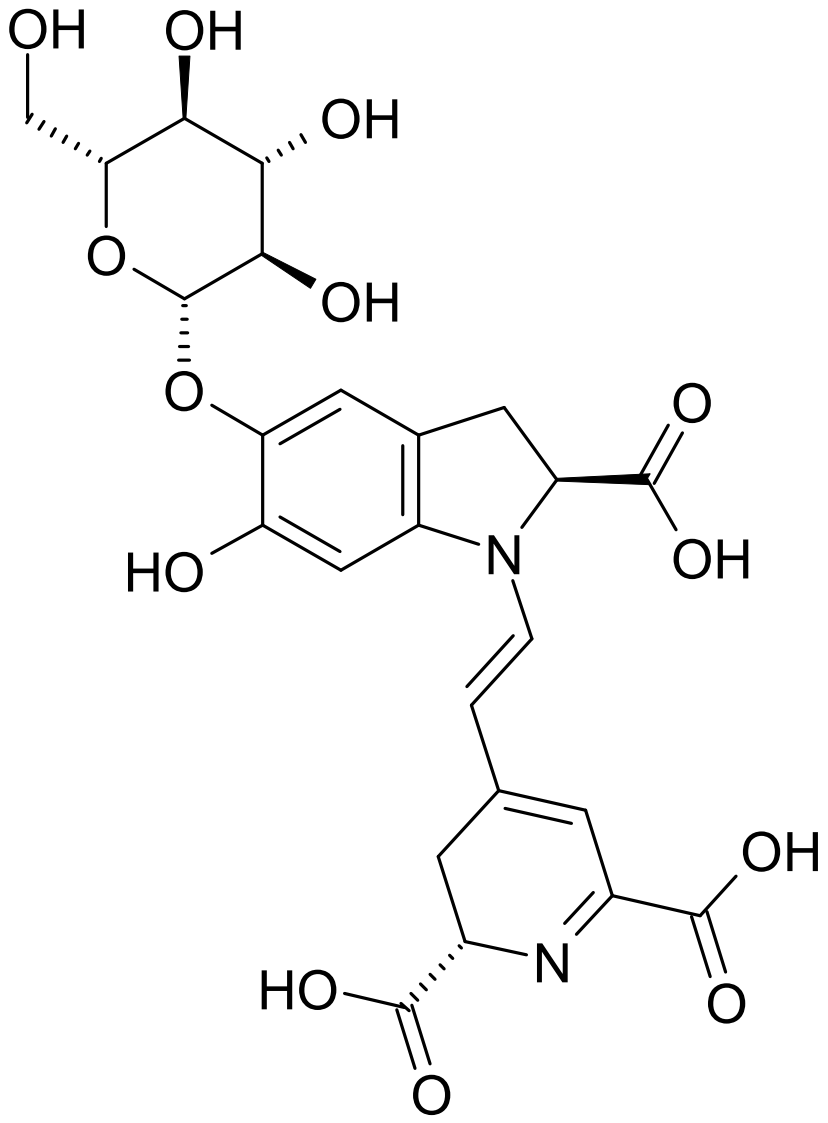
Riboflavine (vitamin B2, lactoflavine)
E 101

- yellow
- listed in PhEur, CzP2009, BP, USP, JP
- Relative absorbance $A_{373\ nm} / A_{267\ nm} = 0.31 – 0.33$, $A_{444\ nm} / A_{267\ nm} = 0.36 – 0.39$



Carmine (= carminic acid, coccinellin, cochineal extract, CI 75470, E 120)

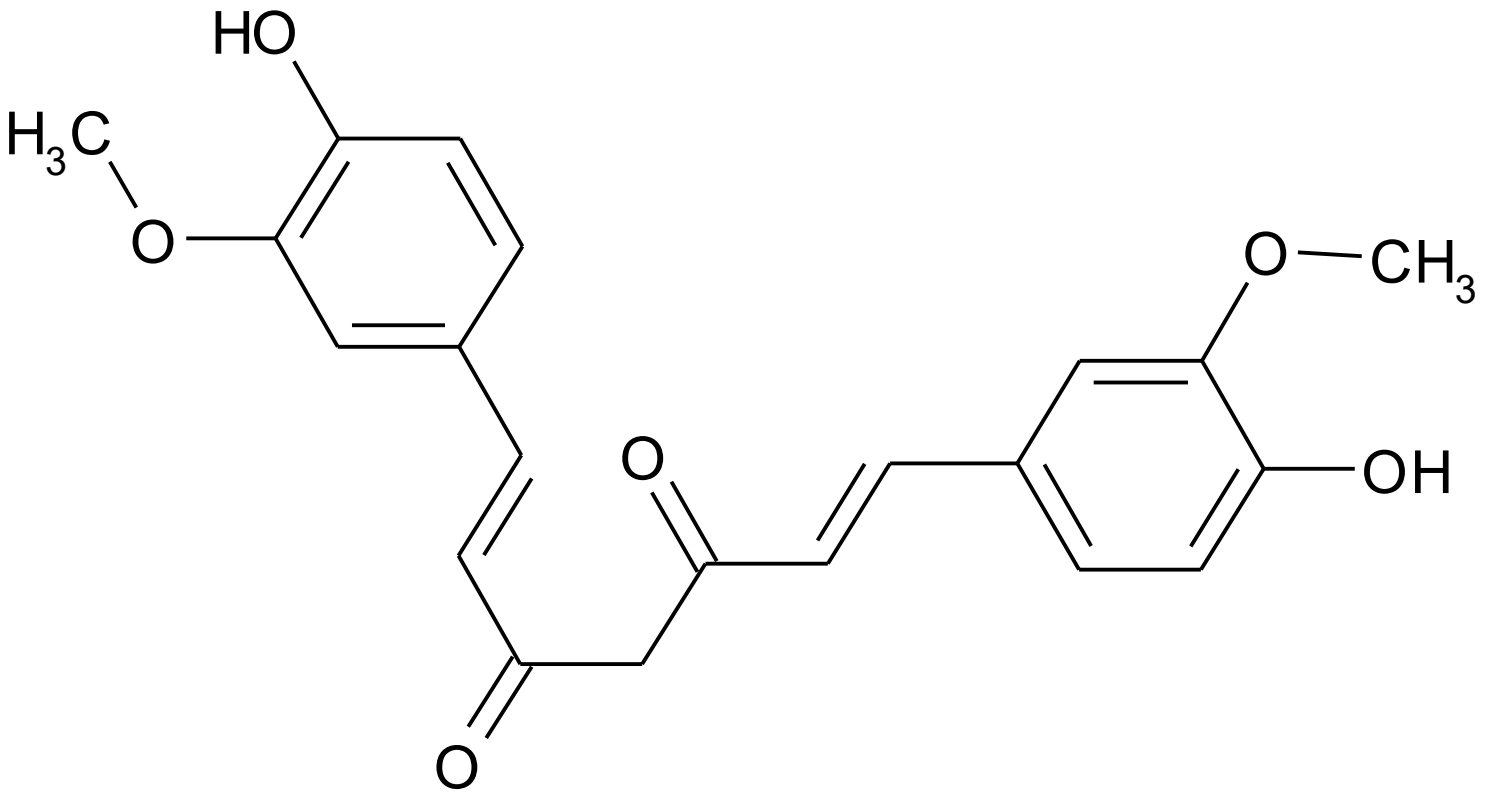
- deeply red
- fruit odour
- water solubility cca 30 g / l
- λ_{max} (buffer pH = 3) = 490 – 493 nm



Betanine, E 162

- *Beta vulgaris* (= beet)
- isolated by water extraction at low temperature

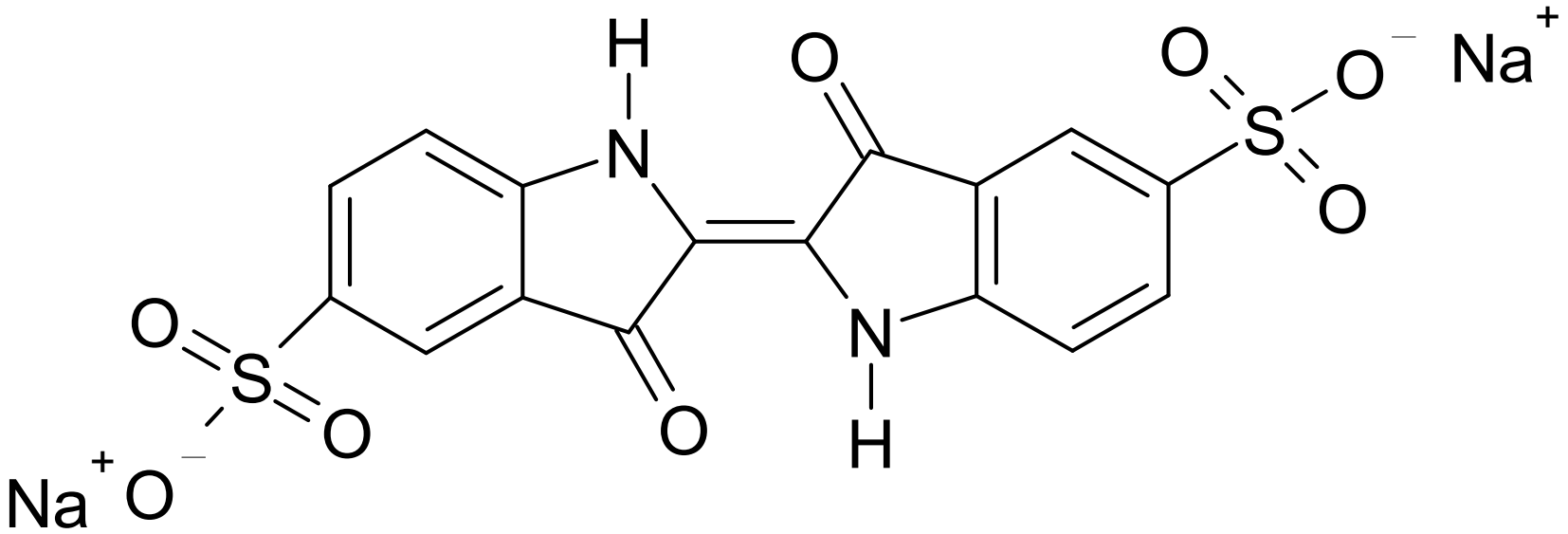
2.2.2 Phenolic dyes not based on fused rings



Curcumin

E 100
- yellow-orange
- approved in EU
- from turmeric root (*Curcuma longa*)

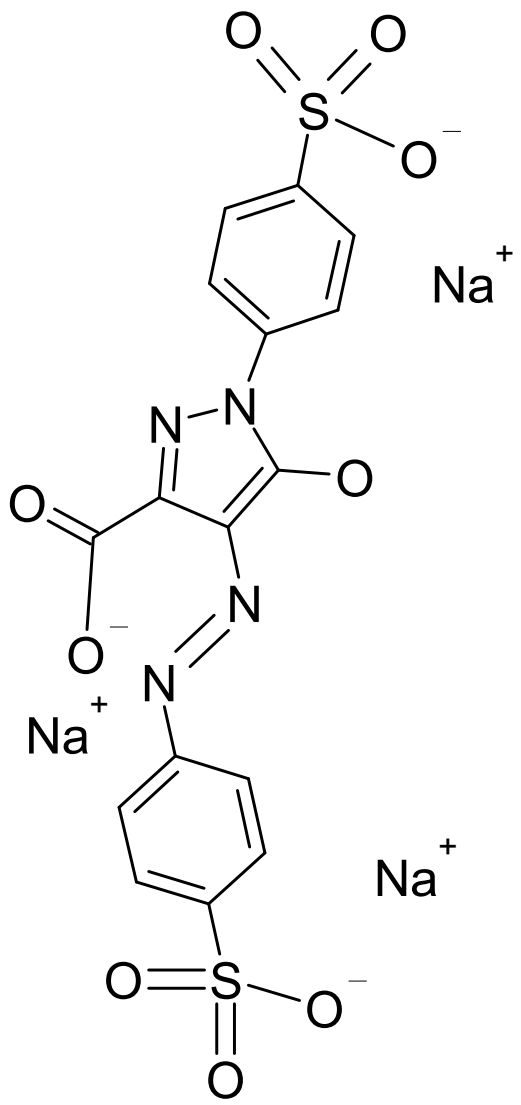
2.2.3 Indole dyes



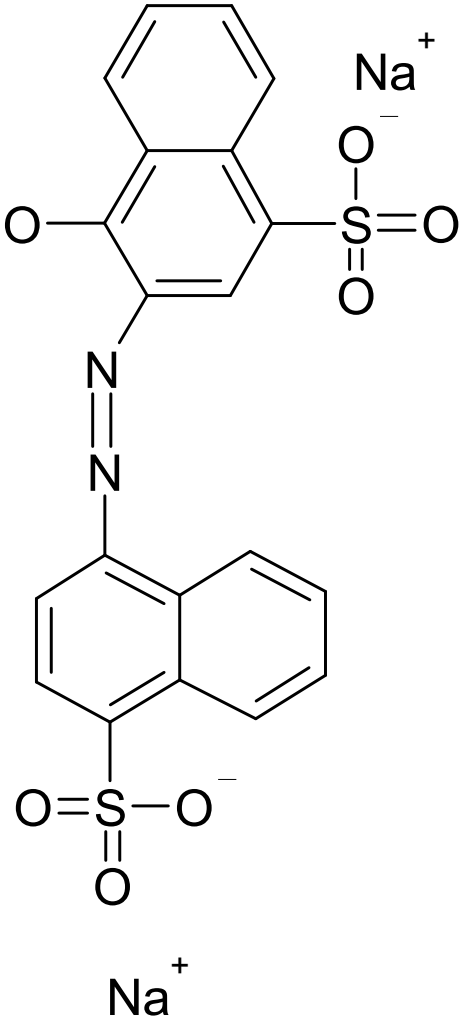
indigo carmine
indigotindisulfonate sodium [USP]
E 132, CI 73015, FD&C blue #2

- deeply blue powder, aqueous solutions are blue or blue-purple
- λ_{max} = 604 nm

2.2.4 Hydrophilic azo-dyes

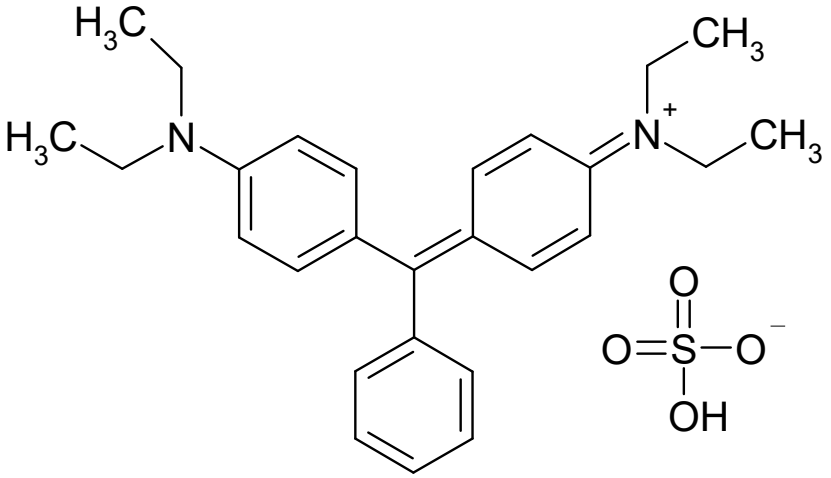


tartrazine, CI 19140, E 102,
acidic yellow 23, egg yellow A
- orange-yellow
- log $P_{octanol/water}$ = -10.17



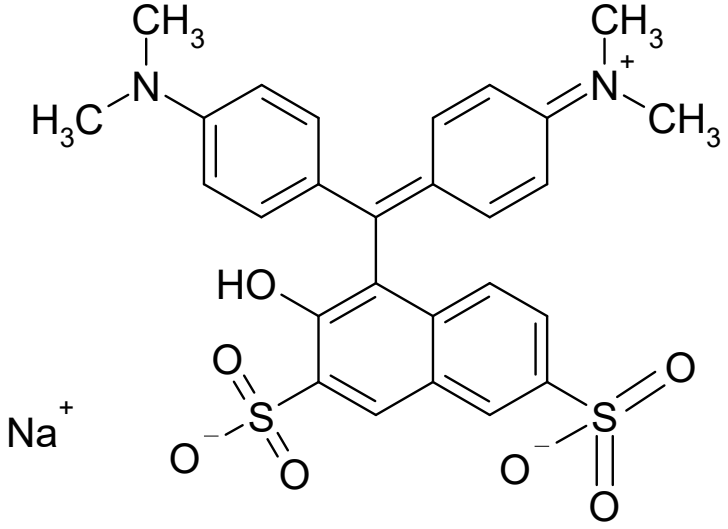
carmoisine, azorubin, E 122,CI 14720,
C.I. Acid Red 14, chromotrop FB
- LD_{50}(*p.o.*, mouse) = 8 g / kg

2.2.5 Hydrophilic triarylmethane dyes

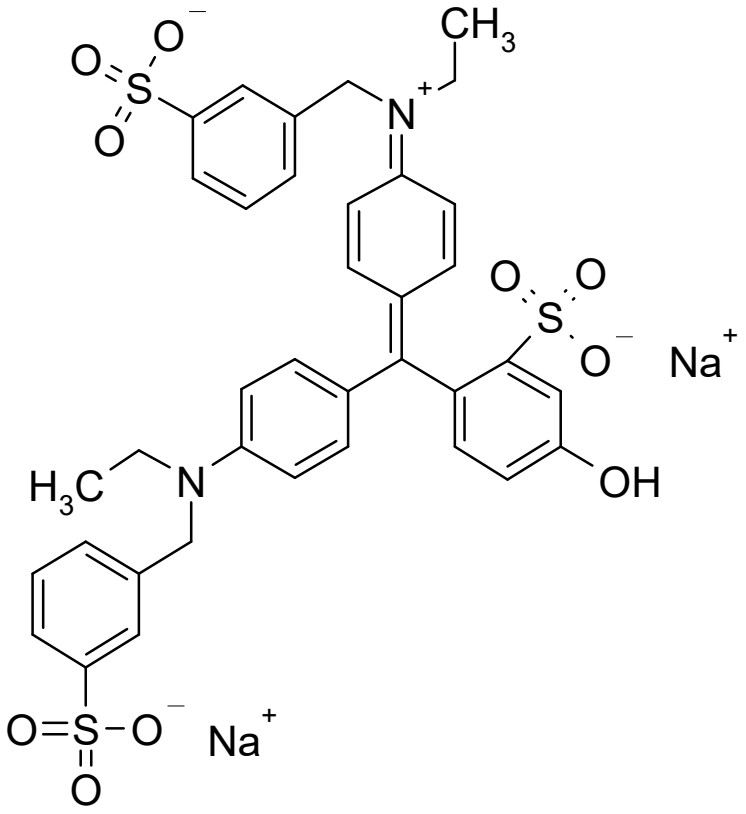


Brilliant Green, CI 42040, *Viride nitens*, Malachite Green G, Emerald Green

- not approved as drug and food dye, but listed in many pharmacopoeias as a therapeutic (antiseptic)
- m.p. 210°C
- log $P_{o/w}$=2.01
- LD_{50} = 3 - 8 mg / kg

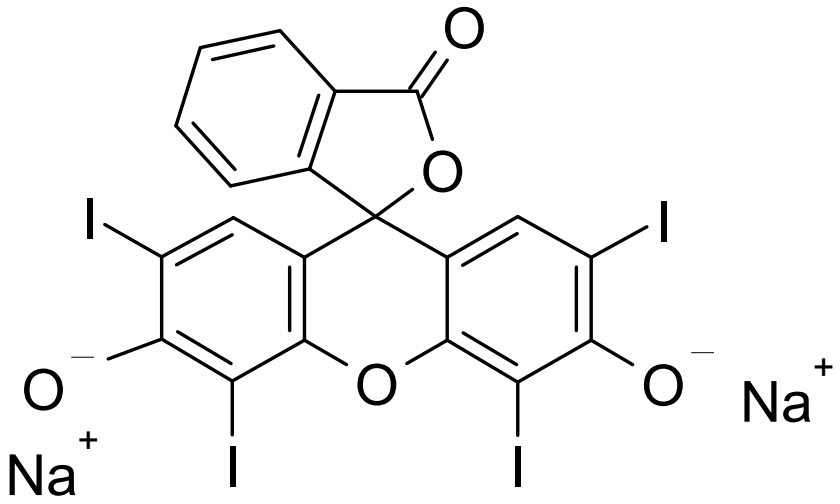


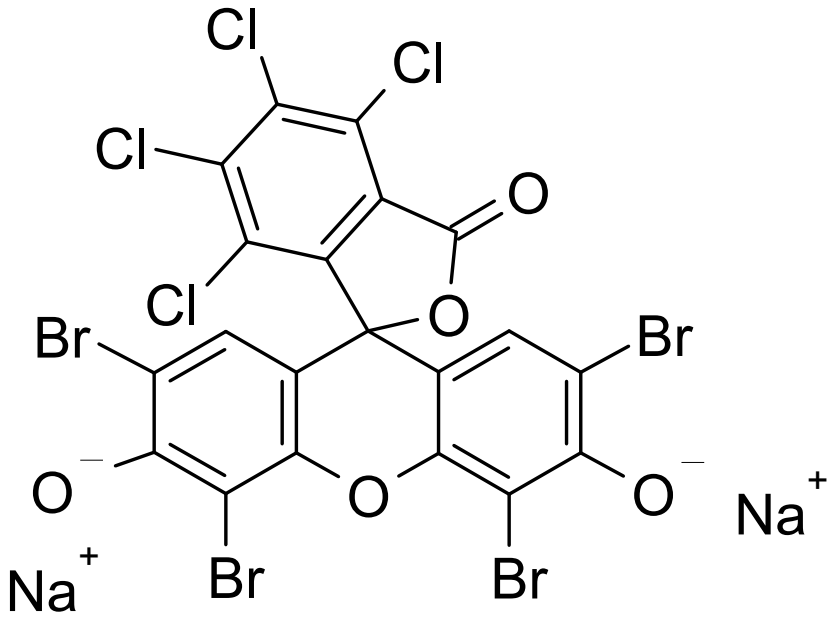
- **Acid Green 50,** Green S, CI 44090, E 142, Brilliant Acid Green BS, Food Green S
- LD_{50} = 2 g / kg



Fast green FCF, CI 42053, Solid Green FCF, Food Green 3

- λ_{max}(ethanol 50 %) 622 - 626 nm
- spec. absorbance $A^{1\%}_{1cm}$ (λ_{max}; 0.003 g/l; ethanol 50%) = 1360 – 1610
- log P o/w = -5.42





Erythrosine (erythrosine B, CI 45430, E 127)

reddish-brown

λ_{max} (water) = 524 - 527 nm

specific absorbance

$A^{1\%}_{1cm}(\lambda_{max}$; 0.005 g/l; water) = 930 - 1170

LD_{50}(*p.o.*, rat) = 1.84 g / kg

Phloxine B (CI45410, D&C red #28, Eosine Blue)

deeply brown

λ_{max} (ethanol 50%) = 546 – 560 nm

$A^{1\%}_{1cm}(\lambda_{max}$; 0.005 g/l; ethanol 50%) = 930 - 1400

LD_{50}(*p.o.*, rat) = 8.4 g / kg