

Chemical synthesis of anthocyanins and investigation of their structural transformations, binding and hydrogen-donating properties in aqueous solution

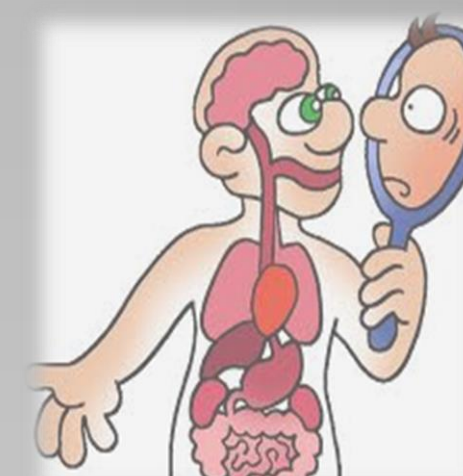
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UMR408, TEAM CHEMISTRY OF ANTIOXIDANTS, UNIVERSITÉ D'AVIGNON ET DES PAYS DE VAUCLUSE, FRANCE



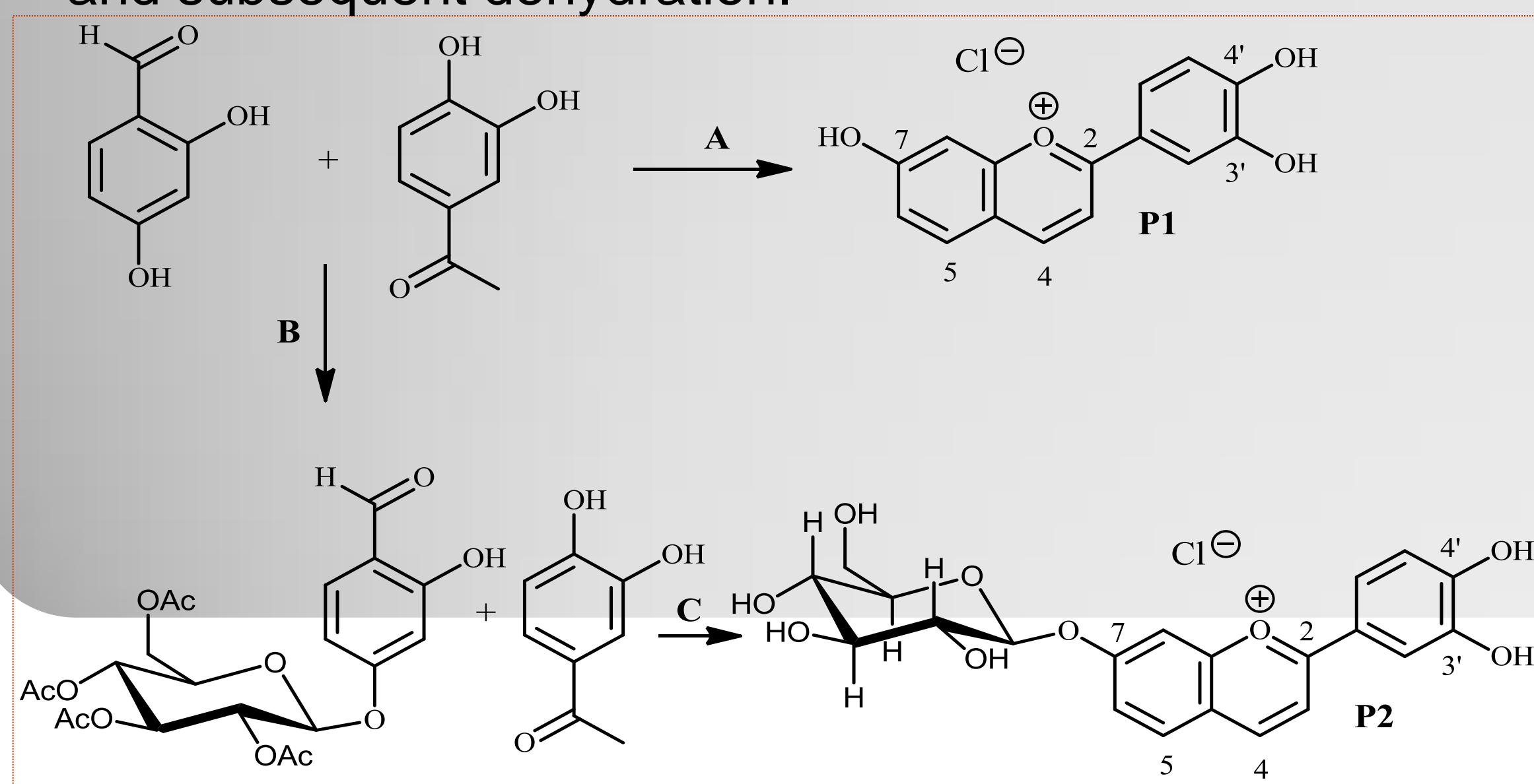
Introduction:

Anthocyanins are naturally occurring glycosides of flavylium (2-phenyl-1-benzopyrylium) ions substituted by hydroxyl and methoxyl groups (1). These polyphenolic pigments are largely responsible for the diversity of red, purple and blue colours of flowers and fruits (2). Polyphenols with a catechol group can bind metal ions and are important antioxidants in plant, food and possibly in humans (3). Our work deals with the chemical synthesis of simple anthocyanin analogues having a catechol group and the investigation of their colouring, metal-binding and antioxidant properties.

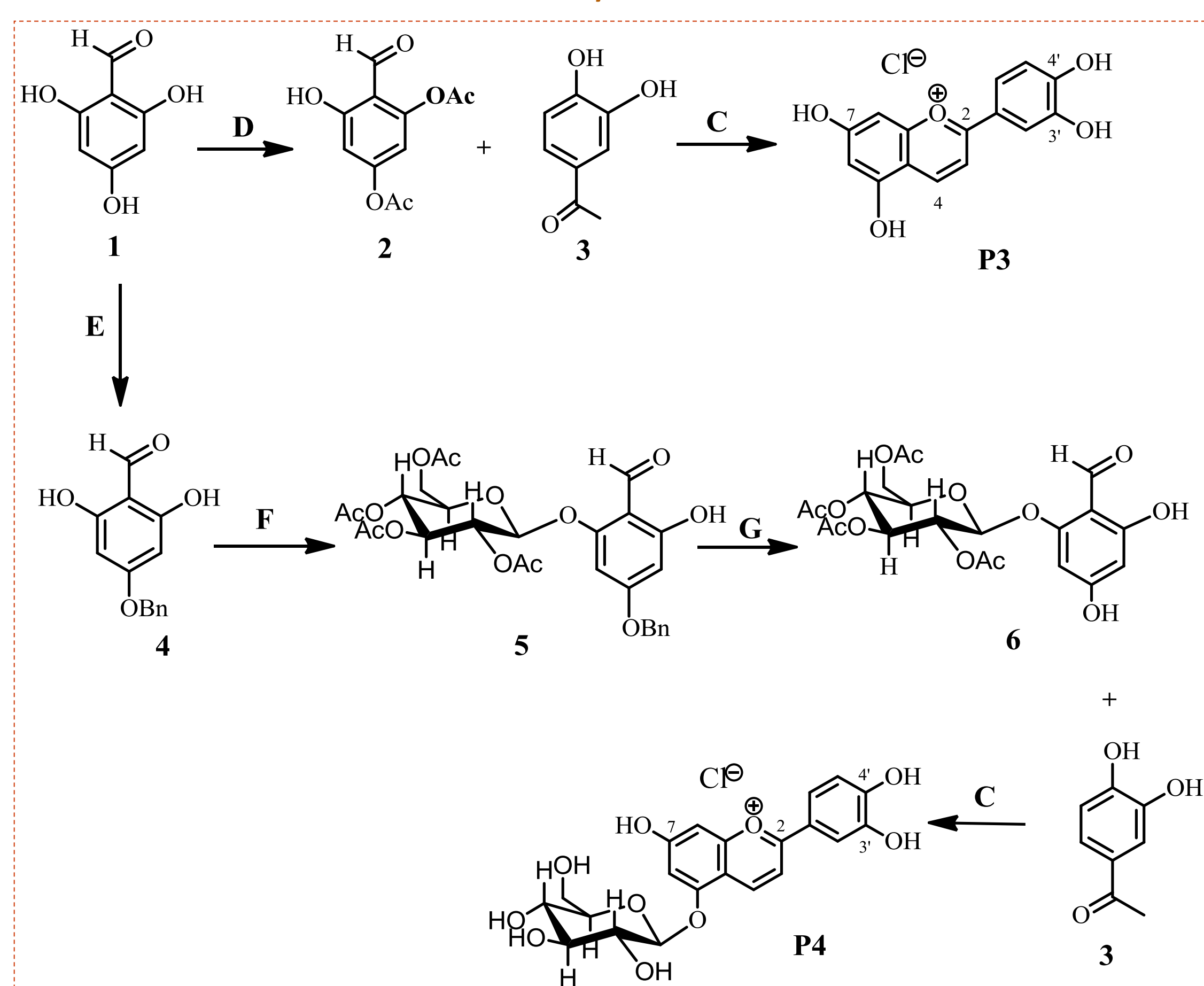


Chemical synthesis of anthocyanins:

The synthesis was adapted from our previous work (4). The critical step is the construction of the chromophore by acid-catalyzed aldol condensation followed by cyclization and subsequent dehydration.



Scheme 1: Chemical synthesis of **P1** and **P2**



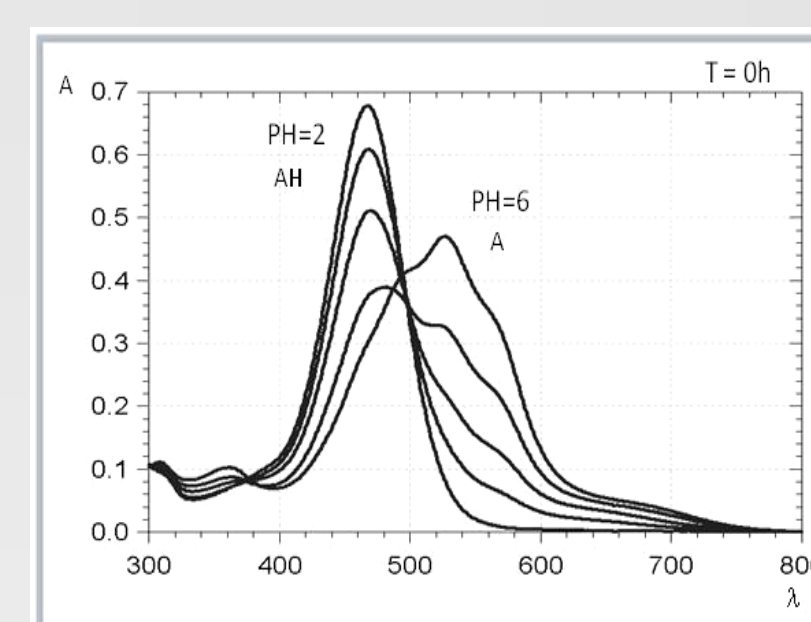
Scheme 2: Chemical synthesis of **P3** and **P4**

- A) Aldol condensation in the presence of HCl gas, 0 °C
 B) Glycosidation: NaHCO₃ + KCl / TMEA, BrGlc(OAc)₄, CH₂Cl₂, reflux, 15h.
 C) Aldol condensation in the presence of HCl gas, 0 °C, MeONa, MeOH, then aq. HCl.
 D) Acetylation: (Ac)₂O, DMAP, AcOEt, reflux, 5h
 E) Benzoylation: DMF, K₂CO₃, BnBr, 0 °C
 F) Glycosidation: K₂CO₃ sat. / TMEA, BrGlc(OAc)₄, CH₂Cl₂, reflux, 15 h
 G) Hydrogenolysis: THF/MeOH (4:1) (v:v), 10% Pd/C, H₂ (2 bars), 0.5 h.

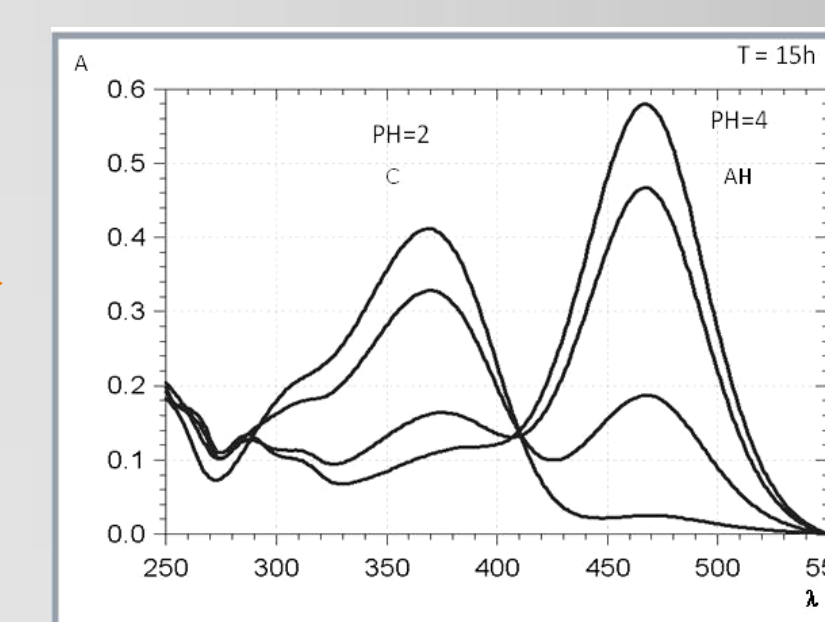
Physico-chemical investigation:

1. Structural transformation in mildly acidic aqueous solution:

P2 appears significantly less acidic than **P1** as a consequence of the replacement of the acidic proton at C7-OH by the β-D-glucosyl moiety (5). However, **P1** and **P2** are equally prone to water addition on the pyrylium ring leading to colourless chalcones.

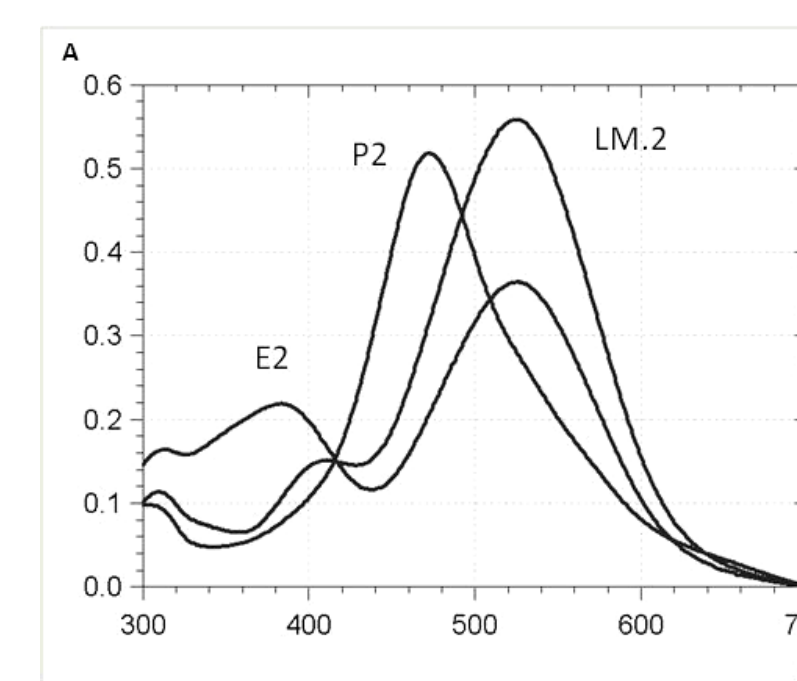
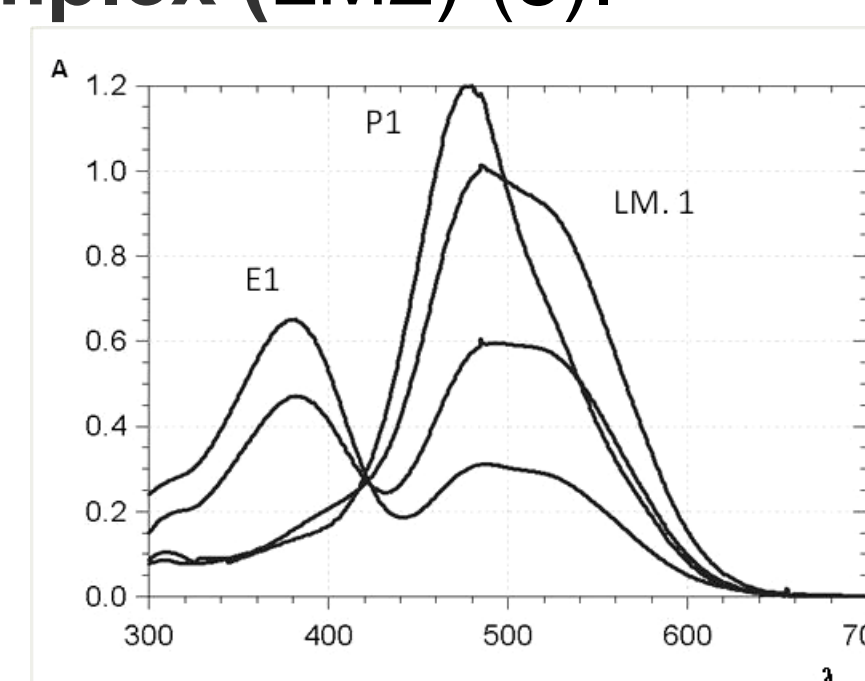


After one night



2. Metal complexation:

Al³⁺ binding is faster with **P1** than with **P2** but the **P1-Al³⁺** complex (LM1) is much more prone to water addition, and thus less stable, than the **P2-Al³⁺** complex (LM2) (5).



3. Antioxidant activity (reduction of the stable DPPH radical):

P1 transfers a first H-atom from its catechol ring to the DPPH radical ca. 4 times as rapidly as **P2**. Moreover, the total number of DPPH radicals reduced by **P1** is ca. 3 times as high as by **P2** (5).

Fig 1: pH-Dependence of the UV-visible spectra of **P2** at time 0 (flavylium – quinonoid base equilibrium).
 Fig 2: pH-Dependence of the UV-visible spectra of **P2** after one night (flavylium – chalcone equilibrium).
 Figs 3,4: UV-visible spectra of **P1** and **P2** respectively, before and after addition of **Al³⁺** at pH 4 and different time points showing maximal metal binding LM and subsequent appearance of free chalcone CE.

Conclusions:

Anthocyanin analogues **P1** and **P2** are stable, easily accessible pigments. The glucose moiety in **P2** increases the water solubility, stabilizes its **Al³⁺** complex but lowers the antioxidant activity.

Perspectives:

Luteolinidin (**P3**) and its O-5 glucoside (**P4**) are anthocyanins of red sorghum. Their chemical synthesis is under way (scheme 2). Their stability in water and DPPH-reducing activity will be estimated.

The 4 anthocyanins will also be investigated for their affinity for iron ions and the protein serum albumin (their likely carrier in the blood circulation) as well as for their ability to inhibit the oxidation of polyunsaturated fatty acids induced by dietary iron, a mechanism for the antioxidant activity of anthocyanins in the stomach.

References:

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