

Supplementary

# Metal–Flavonoid Interactions—From Simple Complexes to Advanced Systems

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**Abstract:** For many years, metal-flavonoid complexes have been widely studied as part of drug discovery programs, but in the last decade, their importance in materials science has increased significantly. A deep understanding the role of metal ions and flavonoids in constructing simple complexes and more advanced hybrid networks will facilitate the assembly of materials with tailored architecture and functionality. In this review, we highlight the most essential data on metal–flavonoid systems, presenting a promising alternative in the design of hybrid inorganic–organic materials. We focus mainly on systems containing Cu<sup>II/I</sup> and Fe<sup>III/II</sup> ions, which are necessary in natural and industrial catalysis. We discuss two kinds of interactions that typically ensure the formation of metal-flavonoid systems, namely coordination and redox reactions. Our intention is to cover the fundamentals of metal-flavonoid systems to show how this knowledge has been already transferred from small molecules to complex materials.

**Keywords:** hybrid materials; redox; flavonoids; transition metals

**Table S1.** Structural and physicochemical details on Cu<sup>II</sup>/Cu<sup>I</sup>-flavonoid systems established by coordination or redox interactions.

| Cu <sup>II</sup> /Cu <sup>I</sup> -flavonoid interaction |   |  |   |      |  |  |      |
|--|---|--|---|------|--|--|------|
| Studied system   | Coordination  |  |   | Ref. | Studied reaction   | Redox  |      |
|  | Coordination sites  | Conditions                                   | Physicochemical data  |      |  | Conditions   | Ref. |
| Cu <sup>II</sup> -naringenin                             | 4-C=O/5-OH  | H <sub>2</sub> O-DMF mixture or DMF solution | UV-Vis: band II at $\lambda_{\max}$ = 290 nm<br>charge transfer transitions at $\lambda_{\max}$ = 360 nm                                      | [49] | Cu <sup>II</sup> + e <sup>-</sup> $\rightleftharpoons$ Cu <sup>I</sup> catalysed by naringenin | pH 4.50 and 5.50 established with acetate buffer<br>pH 6.80 and 7.50 established with HEPES or Tris-HCl buffer; gradual and rising profile of reaction specifically at higher pH | [64] |
|  | 2x naringenin <i>via</i> 4-C=O/5-OH & H <sub>2</sub> O or DMF | Solid phase                                  |   | [49] |  |  |      |
| Cu <sup>II</sup> -apigenin                               | 4-C=O/5-OH  | DMSO or MeOH solution                        | UV-Vis: hypsochromic shift in band II and bathochromic shift in band I  | [22] | Cu <sup>II</sup> + e <sup>-</sup> $\rightleftharpoons$ Cu <sup>I</sup> catalysed by apigenin   | pH 4.50 and 5.50 established with acetate buffer<br>pH 6.80 and 7.50 established with HEPES or Tris-HCl buffer; gradual and rising profile of reaction specifically at higher pH | [64] |
| Cu <sup>II</sup> -luteolin                               | 4-C=O/5-OH & 3'-OH/4'-OH                                      | 0.16 M NaCl solution                         | UV-Vis: hypsochromic shift in band II ( $\Delta \sim 15$ nm)  | [52] | Cu <sup>II</sup> + e <sup>-</sup> $\rightleftharpoons$ Cu <sup>I</sup> catalysed by luteolin   | pH 4.50 and 5.50 established with acetate buffer<br>pH 6.80 and 7.50 established with HEPES or Tris-HCl buffer; bell-shaped response of the reaction yield regardless of pH      | [64] |
|  | pH < 5.00 no coordination<br>pH 5.00-5.80 4-C=O/5-OH          |  | UV-Vis at pH 5.00-5.80: hypsochromic shift in band II and new peak at 290 nm; band I unchanged  | [14] |  |  |      |
|  | pH 6.00-7.20 3'-OH/4'-OH                                      |  | UV-Vis at pH 6.00-7.20: hypsochromic shift in band II ( $\Delta \sim 60$ nm) and bathochromic shift in band I ( $\Delta \sim 4$ nm)           |      |  |  |      |
| Cu <sup>II</sup> -kaempferol                             |   |  | EPR in DMSO at 100K<br>$g_{\perp} = 2.073$<br>$g_{\parallel} = 2.291$ $A_{\parallel} = 125$ and $g_{\parallel} = 2.242$ $A_{\parallel} = 118$ |      | Cu <sup>II</sup> + e <sup>-</sup> $\rightleftharpoons$ Cu <sup>I</sup> catalysed by kaempferol | pH 4.50 and 5.50 established with acetate buffer<br>pH 6.80 and 7.50 established with HEPES or Tris-HCl buffer; bell-shaped response of the reaction yield regardless of pH      | [64] |
|  | 4-C=O/5-OH in DMSO<br>4-C=O/3-OH in MeOH                      | DMSO and MeOH solution                       | UV-Vis in DMSO at RT: new band at 290 nm  | [22] |  |  |      |
|  |   |  | UV-Vis in MeOH at RT: minor shift in band II ( $\Delta \sim 5$ nm); shift in band I ( $\Delta \sim 65$ nm)                                    |      |  |  |      |

|                             |  |   |  |  |   |   |  |      |
|-----------------------------|--|---|--|--|---|---|--|------|
| Cu <sup>II</sup> -quercetin | mononuclear complex 4-C=O/3-OH in MeOH                           | MeOH solution and DMSO-d <sub>6</sub> for <sup>1</sup> H- NMR | UV-Vis of binuclear complex: bathochromic shift in band I and II   | [55]   | Cu <sup>II</sup> + e <sup>-</sup> ⇌ Cu <sup>I</sup><br>catalysed by quercetin | pH 7.50 at various M:L 1:1, 2:1, and 3:1  | [66,67]  |      |
|                             | binuclear complex 4-C=O/3-OH and 3'-OH/4'-OH in MeOH             |   | <sup>1</sup> H-NMR: pure quercetin δ 9.60 (s, <sup>1</sup> H, 3-OH) and lack of this signal in binuclear complex |  |   |   |  |      |
|                             |  |   |  |  | Cu <sup>II</sup> + e <sup>-</sup> ⇌ Cu <sup>I</sup><br>catalysed by quercetin | pH 4.50 and 5.50 established with acetate buffer<br>pH 6.80 and 7.50 established with HEPES or Tris-HCl buffer; bell-shaped response of the reaction yield regardless of pH | [64]   |      |
|                             | mononuclear complex 3'-OH/4'-OH in H <sub>2</sub> O              | H <sub>2</sub> O solution, pH 10.00                           | UV-Vis of mononuclear complex: decrease in the intensity of band I   | [56]   |   |   |  |      |
|                             | binuclear complex 4-C=O/5-OH and 3'-OH/4'-OH in H <sub>2</sub> O |   | UV-Vis of binuclear complex: decrease in the intenisty of band I and band II                                     |  |   |   |  |      |
|                             | 3'-OH/4'-OH at M:L below 0.0028                                  | H <sub>2</sub> O solution, pH 5.00                            | UV-Vis at M:L below 0.0028: increase in the intensity of band I  | [57]   |   |   |  |      |
|                             | 4-C=O/3-OH at M:L in the range from 0.0028 to 3.2                |   | UV-Vis at M:L in the range 0.0028 – 3.2: bathochromic shift of band II   |  |   |   |  |      |
|                             | Cu <sup>II</sup> -catechin                                       | pH 5.50: no coordination<br>pH 7.40: 3'-OH/4'-O               | H <sub>2</sub> O solution, pH 5.50 and 7.40  | UV-Vis at pH 7.40: bathochromic shift and small decrease in band I (Δ ~ 16 nm) | [15]  | Cu <sup>II</sup> + e <sup>-</sup> ⇌ Cu <sup>I</sup><br>catalysed by catechin  | pH 4.50 and 5.50 established with acetate buffer<br>pH 6.80 and 7.50 established with HEPES or Tris-HCl buffer; gradual and rising profile of reaction specifically at higher pH | [64] |
|                             |  |   |  |  |   |   |  |      |
|                             |  |   |  |  |   | Cu <sup>II</sup> + e <sup>-</sup> ⇌ Cu <sup>I</sup><br>catalysed by catechin  | pH 7.50 at M:L 2:1   | [65] |
| Cu <sup>I</sup> -quercetin  | 4-C=O/3-OH   | MeOH solution   | UV-Vis: bathochromic shift in band I (Δ ~ 24 nm) and band II (Δ ~ 34 nm)   | [70]   |   |   |  |      |

**Table S2.** Structural and physicochemical details on Fe<sup>III</sup>/Fe<sup>II</sup>-flavonoid systems established by coordination or redox interactions.

| Fe <sup>II</sup> /Fe <sup>III</sup> -flavonoid interaction |   |   |   |      |   |  |      |
|--|---|---|---|------|---|--|------|
| Studied system   | Coordination  |   |   | Ref. | Studied reaction  | Redox  |      |
|  | Coordination sites  | Conditions  | Physicochemical data  |      |   | Conditions   | Ref. |
| Fe <sup>III</sup> -naringenin                              | 4-C=O/5-OH  | H <sub>2</sub> O solution, 0.5 M NaClO <sub>4</sub><br>ionic strength,<br>25°C, pH range 1–3  | Kinetic studies based on UV-Vis   | [95] | Fe <sup>II</sup> - e <sup>-</sup> ⇌ Fe <sup>III</sup><br>catalysed by narin-<br>genin | H <sub>2</sub> O solution at pH 6.50 and 7.00                                | [59] |
|  | 4-C=O/5-OH  | H <sub>2</sub> O solution, pH 6.50  | UV-Vis: bathochromic shift in band I<br>(λ <sub>max</sub> = 350 nm, sh)   | [60] |   | DMSO solution  | [69] |
| Fe <sup>III</sup> -apigenin                                | 4-C=O/5-OH  | H <sub>2</sub> O solution, pH 2.00  | UV-Vis: Ligand-to-Fe <sup>III</sup> -Charge Transfer (LMCT)<br>transitions (λ <sub>max</sub> = 520 nm); bathochromic shift in<br>band I and II  | [59] | Fe <sup>III</sup> + e <sup>-</sup> ⇌ Fe <sup>II</sup><br>catalysed by luteolin        | H <sub>2</sub> O solution, 90°C  | [70] |
| Fe <sup>III</sup> -luteolin                                | 3'-OH/4'-OH   | EtOH solution   | UV-Vis: bathochromic shift in band I and II   | [61] |   |  |      |
|  | 3'-OH/4'-OH   | H <sub>2</sub> O solution, pH 6.50  | UV-Vis: bathochromic shift in band I (λ <sub>max</sub> = 420<br>nm) and II (λ <sub>max</sub> = 270 nm) and new band from<br>π <sub>π</sub> →d <sub>π</sub> LMCT (λ <sub>max</sub> = 550 nm) | [60] |   |  |      |
| Fe <sup>III</sup> -kaempferol                              | 4-C=O/5-OH  | H <sub>2</sub> O solution, pH 4.00 and<br>8.00  | UV-Vis: bathochromic shift in band I  | [62] |   |  |      |
|  | 4-C=O/5-OH  | H <sub>2</sub> O solution, pH 6.50  | UV-Vis: bathochromic shift in band I<br>(λ <sub>max</sub> = 420 nm)   | [60] |   |  |      |
| Fe <sup>II</sup> -quercetin                                | 4-C=O/5-OH  | MeOH solution   | UV-Vis: bathochromic shift in band I and band<br>II; new band from π <sub>π</sub> →d <sub>π</sub> LMCT (λ <sub>max</sub> = 425 nm)  | [78] | Fe <sup>III</sup> + e <sup>-</sup> ⇌ Fe <sup>II</sup><br>catalysed by quercetin       | MeOH-H <sub>2</sub> O mixture 1:1 with 0.1 % ace-<br>tic acid; final pH 3.00 | [71] |
| Fe <sup>III</sup> -quercetin                               | 3'-OH/4'-OH in the dominant<br>species Fe(H) <sub>5</sub> (H <sub>5</sub> Que) <sub>2</sub> <sup>2-</sup> | H <sub>2</sub> O solution, pH range 2.00-<br>4.50, 0.16 M NaCl, 37°C<br>Fe(H) <sub>5</sub> (H <sub>5</sub> Que) <sub>2</sub> <sup>2-</sup> species<br>with M:L 1:2, pH 2.00<br>Fe(H) <sub>4</sub> (H <sub>5</sub> Que) <sup>-</sup> with M:L 1:1,<br>pH 3.00<br>Fe(H) <sub>6</sub> (H <sub>5</sub> Que) <sub>2</sub> <sup>3-</sup> with M:L<br>1:2, pH 3.00 | Potentiometric titration and DFT  | [80] |   |  |      |
|  |   |   |   |      |   |  |      |
|  |   |   |   |      |   |  |      |
|  | 4-C=O/3-OH  | DMSO-d <sub>6</sub>   | <sup>1</sup> H-NMR, <sup>13</sup> C-NMR and maps of the molecular<br>electrostatic potential (MEP)  | [80] | Fe <sup>III</sup> + e <sup>-</sup> ⇌ Fe <sup>II</sup><br>catalysed by quercetin       | 0.1 M HCl-MeOH 1:1, 37°C   | [72] |
|  |   |   |   |      | Fe <sup>III</sup> + e <sup>-</sup> ⇌ Fe <sup>II</sup><br>catalysed by quercetin       | MeOH-H <sub>2</sub> O mixture 1:1 under aerobic<br>and anaerobic atmosphere  | [74] |

|                                    |             |                           |  |      |  |  |      |
|------------------------------------|-------------|---------------------------|--|------|--|--|------|
|                                    |             |                           |  |      | $\text{Fe}^{\text{III}} + \text{e}^- \rightleftharpoons \text{Fe}^{\text{II}}$<br>catalysed by quercetin | 50 mM acetate buffer, pH 5.50                                | [15] |
| $\text{Fe}^{\text{III}}$ -catechin | 3'-OH/4'-OH | aqueous solution, pH 7.40 | UV-Vis; new LMCT band at $\lambda_{\text{max}} = 491 \text{ nm}$ , pH range 9.71-10.10 and $\lambda_{\text{max}} = 551 \text{ nm}$ , pH 7.40 | [82] | $\text{Fe}^{\text{III}} + \text{e}^- \rightleftharpoons \text{Fe}^{\text{II}}$<br>catalysed by catechin  | nano-ESI-MS analysis; MeOH- $\text{H}_2\text{O}$ mixture 1:1 | [54] |