Synthesis, Characterization, and DNA-binding properties of La(III) complex of chrysin.

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Introduction

• Chemicals exert antitumor effects through DNA binding.
• Synthesis of metallic antitumor reagents is based on the mode and affinity of the binding.
• La(III) complex is metallic antitumor reagent (Lanthanum & Chrysin)
• Interactions done with calf thymus DNA.

Experimental

• Preparation of La(III) complex
  – CaC\textsubscript{2}Cl\textsubscript{2} 1mmol chrysin & 10ml ethanol in 50ml round-bottom flask with electromagnetic stirrer & CaC\textsubscript{2} guard tube. Heat to 90°C on oil bath & dissolve chrysin. Add NaOH(s) & then La(III) acetate-str & boil under reflux for 7-8hr. Cool to room temp. and yellow precipitate forms. Wash with ethanol-water and dry in vacuo for 48h.

Results and Discussion

• Composition & Properties of Complex
  – chrysin & acetate ion act as bidentate ligand
  – form mononuclear complex
  – La(III) ion bound to two chrysin with one acetate ion as synergistic anion
• elemental analyses done by IR & H NMR measurements.
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**IR Spectra / H NMR**
- Transition of chrysin into La(III) complex, c=0 vibration went from 1655 to 1638 cm⁻¹.
- Symmetric & asymmetric stretching vibration of carboxyl grp (1541 & 1490 cm⁻¹).
  - Suggests bidentate coordination.
- Compared with chrysin H NMR, La(III) complex showed (5-OH) hydroxy proton disappeared (12.82 ppm).
  - Broad single peak at 1.61 ppm from the methyl proton (CH₃CO₂⁻).
  - Indicates O⁻ and CH₃CO₂⁻ are coordinated to La(III).

**La(III) complex with ctDNA**
- Absorption spectra
  - La complex concentration (10uM) & varied nucleic acid concentration (10-50uM)
  - Π→Π* transition at 274 nm of the La(III) complex
  - Indicates strong Π-stacking interaction between the complex and DNA base pairs.
  - Thus, complex inserts into DNA more deeply.
  - Binding modes of complex and chrysin are the same, but binding affinities to DNA are different.
La (III) complex with ctDNA

- viscosity measurement
  - intercalation model results in lengthening the DNA helix as base pairs are separated to accommodate the complex.
  - Increases DNA viscosity.
  - Changing temperature from 15.0 to 35.0°C shows viscosity of La(III) complex decreases as temp. increases. Why?

Antitumor Activity

- National Centre for Drug Screening
- Inhibiting effects of La (III) complex and chrysin against 2 tumor cells (A-549 and P388) were studied
- La (III) complex at 10μM had higher inhibitory effect than chrysin
- Antitumor activity in accordance with experiment

Table 1

| Inhibitory effect against A-549 tumor cell (using DMF as solvent control) | Inhibitory effect (%) |
|---|---|---|---|---|---|
| 100 μM | 10 μM | 1 μM | 0.1 μM | 0.01 μM |
| Chrysin | 95.1 | 4.9 | – | – | – |
| La(III) complex | 89.8 | 73.5 | – | – | – |

Table 2

| Inhibitory effect against P388 tumor cell (using DMF as solvent control) | Inhibitory effect (%) |
|---|---|---|---|---|---|
| 100 μM | 10 μM | 1 μM | 0.1 μM | 0.01 μM |
| Chrysin | 71.3 | 60.7 | 8.7 | 0.9 | 7.3 |
| La(III) complex | 71.2 | 42.4 | 6.0 | 0.5 | 1.6 |
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Summary

- La (III) complex of chrysin (5,7-dihydroxyflavone) was synthesized and characterized
- Interactions of La (III) complex with calf thymus DNA
- Intercalation modes occurs
- Binding affinity is higher for La (III) complex than chrysin.
- La (III) complex can inhibit tumor growth