Synthesis of a library of curcumin derivatives with potential P-gp modulatory activity

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INTRODUCTION

Curcumin → Several biological activities → Downregulates mdr1 gene → Decreases cellular levels of P-gp

RESULTS AND DISCUSSION

- Three building blocks similar to curcumin were synthesized, with smaller linkers between the two aromatic rings:
  - Dienone [2]
  - Cyclohexane [2]
  - N-methyl-piperidine [3]

- Dienone 1 derivatives were synthesized with different substitution patterns in the phenolic groups via Sn2 (reaction conditions i) from Scheme 3) or Ullmann’s reaction (reaction conditions ii) from Scheme 3) [4,5]:
  - The substituents chosen were mostly secondary and tertiary amines, sugars, and alkyl groups;
  - Structure elucidation of the compounds was achieved by 1H NMR and 13C NMR.

CONCLUSIONS AND FUTURE WORK

- We were able to synthesize several curcumin derivatives with a shorter linker (3 building blocks) and with different substitutions patterns in the phenolic groups (11 new compounds)
- The structure elucidation of some of the synthesized compounds (2, 3, 8, 10, 12 and 14) is ongoing.
- The main focus of the biological tests of such derivatives will be towards cytotoxicity and modulation of P-gp expression in human tumor cell lines.

REFERENCES


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