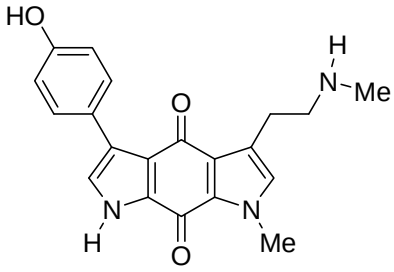
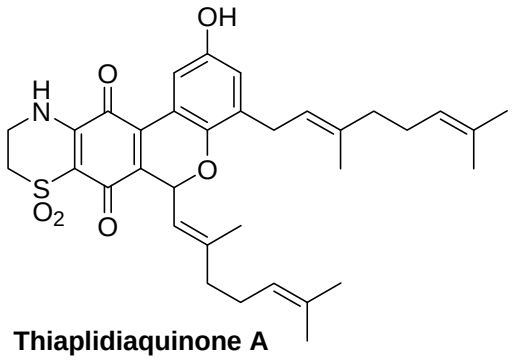
Final Publishable Summary Report – Nabio (252173)

The original proposal was inspired by a need for safer and more effective medicines, particularly for the treatment of cancer. One of the most successful methods for drug discovery is based on materials from Nature: "natural products". The project was therefore based on "Medicines from Nature", an attractive concept in terms of the European public perception of drug research.

The two targets described in the original proposal were the two natural compounds: **zyzzyanone A** and **thiaplidiaquinone A** (Figure 1), compounds that are reported to possess antitumour activity. However, their biological properties have not been fully evaluated to date due to lack of material, and there have been no synthetic approaches to these compounds described.



Zyzzyanone A



Thiaplidiaquinone A

Figure 1.

In order to address the synthesis of such molecules, we elected to find new synthetic methodology for the construction of heterocyclic rings. In particular, we developed a new variation of the Fischer reaction to obtain the "indole core" of the **zyzzyanone A**, and used a biosynthesis-inspired route to pyranoquinones that employs a facile 6π-electrocyclic process to obtain the "pyranoquinone core" of the **thiaplidiaquinone A**.

<u>During this Fellowship we obtained the following results:</u>

- Development of new methodology towards the synthesis of indoles by a new variation of the Fischer reaction;
- as a practical application of the present Fischer indolisation method, we have started the synthesis of the anticancer natural product **zyzzyanone A**. Unfortunately one of the last steps of our followed synthetic route failed, and it was not possible to obtain the natural compound;
- total synthesis of **thiapliadiaquinone A** via a facile 6π-electrocyclization;
- published the results in high quality international journals.

In summary, the benefits of the project include:

- The career development of a talented researcher extending a medicinal chemistry background with a strong synthetic organic chemistry knowledge;
- acquisition of additional research and complementary skills in organic chemistry;
- the host laboratory has benefited from a researcher with a medicinal chemistry background;
- a long term collaboration between two complementary European laboratories;
- development of high new chemical synthetic procedures for applications in the EU chemicals industry;
- the development of a talented researcher, a future leader and role model for women;
- helping Europe to remain globally competitive in the area of the chemical sciences.