

## Technical Brief

Ref No: TechBrief/2021/15

### Sustainable production of camptothecin from a high yielding endophyte

#### Technology Summary

A microbial source for the *in vitro* production of the plant derived anti-cancer drug Camptothecin. It is the highest camptothecin-yielding native strain reported till date, and can be used as an alternative to natural plant extraction or chemical synthesis for a fast and sustainable production of camptothecin at large scale to meet the increasing market demand.

#### Background

Camptothecin is an anticancer alkaloid that is commercially produced from plants. It inhibits DNA topoisomerase I in cancer cells leading to cell death. Owing to the high demand of camptothecin, its source plants are endangered and overharvested. Thus, a sustainable means of camptothecin production is needed. Endophytes, the microorganisms that reside within plants, are reported to have the ability to produce host-plant associated metabolites. However, the commercial production of bioactive compounds using endophytes has not yet been established. The bottleneck has been the inconsistent product yield, which decreases rapidly with successive subculture under axenic state.

#### Technology Description

Endophytes from *Nothapodytes nimmoniana* were isolated from various parts of the plant, such as leaves, stem, and bark. The isolated endophytes were individually screened for their ability to produce camptothecin in suspension, which was confirmed qualitatively and quantitatively by tandem mass spectrometry (LC-MS/MS), thin layer chromatography (TLC) and high performance liquid chromatography (HPLC). Sustainable production of camptothecin in the two highest camptothecin yielding endophytes was assessed in suspension culture generated from the 1st through the 12th generation slants. The strain (*A. burnsii* NCIM1409) could demonstrate sustainable production of camptothecin in culture even from its 12th generation slant used as inoculum, which was also confirmed via <sup>13</sup>C-labelling of camptothecin extracted from the starved culture grown on fully-labelled glucose. The cytotoxicity of the crude extract of camptothecin from *A. burnsii* was tested on various cancer cell lines, including breast, ovarian, lung etc. The microbial production platform developed is amenable to optimisation and scale-up to achieve maximum productivity of camptothecin at large scale.

#### Market Potential

The global oncology drugs market was valued at \$128 billion in 2019, and is projected to reach \$222 billion by 2027, at a CAGR of 7.4%. Camptothecin market is probably in the range of 500- 1000 m\$.

#### Value Proposition

- Sustainable production of Camptothecin in axenic state (~2 mg/L; 250 µg/L/d) in batch
- Uniform and consistent product quality with less impurities than in natural plant extracts
- Faster, cost effective, continuous production with better yield
- 100% similarity to marketed/plant derived camptothecin molecule
- Microbial source is non-pathogenic to healthy humans
- Highest yield in any native strain of endophyte reported to date
- Camptothecin extract demonstrates high sensitivity to Colon, Ovary and Lung cancer

#### Applications

The camptothecin topoisomerase I-targeting agents are new class of antitumor drugs with demonstrated clinical activity in human malignancies, such as colorectal cancer and ovarian cancer

#### Technology Status

- Demonstrated at lab scale using a 3 L fermenter
- Patent protected
- Seeking interested industry partners

#### References

Sustainable production of camptothecin from an *Alternaria* sp. isolated from *Nothapodytes nimmoniana*. I.A. H. Khwajah Mohinudeen, Rahul Kanumuri, K. N. Soujanya, R. Uma Shaanker, Suresh Kumar Rayala & Smita Srivastava. Sci. Rep. (Nature research publication) (2021) 11:1478.

<https://www.alliedmarketresearch.com/oncology-cancer-drugs-market>

