Production of Prolyl Oligopeptidase Inhibitor Via Repeat Batch Culture of Immobilized *Fusarium* sp. CMI397470

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Abstract

Fusarium sp. CMI397470 is a producer of inhibitor of Prolyl Oligopeptidase (POPI). Since the pattern of POPI production by this fungus is growth-dissociated, via immobilized mycelium was thought viable and shown to be so. Various medium ranging from simple chemical defined to complex combination, were tested for it suitability for the production of the metabolites. The most suitable medium for the POPI is a defined medium with glucose the carbon source at 60 g L^{-1}. POPI production was found to be sustainable over 6 sequential batch cultures in a period totaling 46 days.

Keywords

Prolyl oligopeptidase inhibitor · Alzheimer's · *Fusarium* · fermentation

Introduction

Abnormal mammalian prolyl oligopetidase (POP) activity has been linked to neurological disorders (Lawandi *et al.* 2010). For example, POP is found in elevated levels in the brains of patients with Alzheimer's Disease (Aoyogi *et al.* 1990). Inhibition of POP activity as a strategy to ameliorate neurological disorders has received a lot of research attention (Lawandi *et al.* 2010) and has been shown to be successful in animal models (Morain *et al.* 2002).

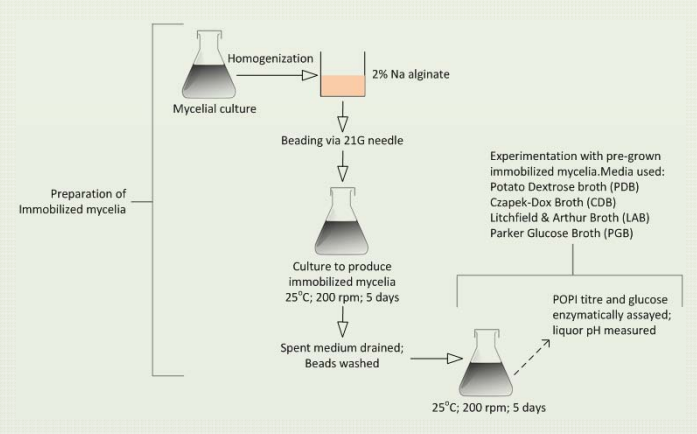
Culture liquor from endophytic fungus isolated from a plant near Kuching, Sarawak showed inhibitory activity against POP. The fungus was identified as a *Fusarium* sp. and assigned a collection number, CMI397470 (CABI, Bakeham Lane, Egham, Surrey, TW20 9TY, United Kingdom).

The production of POPI by CMI 397470 has been characterized as growth-dissociated in previous study (Ng *et al.* 2011). This means that production of POPI via repeat batch culture using immobilized mycelia of CMI397470 should be possible.

Aims:

- To confirm production of POPI via immobilization of mycelia.
- To compare production using 4 different media.
- To determine an optimal glucose concentration.

Materials and Methods



Results and Discussion

Production of POPI in different media

- Parker Glucose Broth gave the best yield (Fig. 1).
- Pre-grown immobilized mycelium prefers weak, simple medium to produce POPI.

The effect of glucose quantity in Parker Glucose Broth on POPI production

- In the range 5 – 60 g L^{-1}, the higher the glucose amount supplied, the better the yield obtained (Fig. 2).
- There appears to be acclimation through repeated use of the immobilized mycelia because the glucose effect was more pronounced in the 2nd and 3rd culture batches.
- Although 60 g L^{-1} resulted in the highest titre, the glucose effect appeared to be tapering (Fig. 2b and 2c).

- Pre-grown immobilized mycelia as used in this study are unlikely to require for growth, the reported amounts of glucose supplied to it.
  - At 60 g L-1, glucose is not completely consumed in the fermentation (Fig. 3).
  - At 40 g L-1, the is acclimation to glucose as its complete exhaustion is achieved only through use of the mycelia in repeated batch cultures.
- It is possible that high glucose concentrations favor POPI production via physical influence such as osmolality.

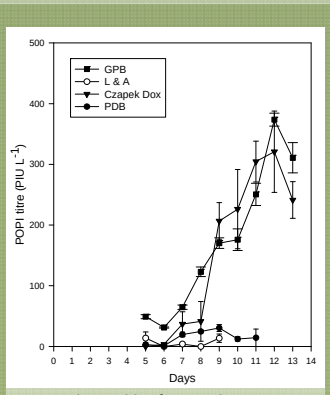


Fig. 1 The yield of POPI by pre-grown immobilized Fusarium sp. CMI397470 obtained using 4 different media.

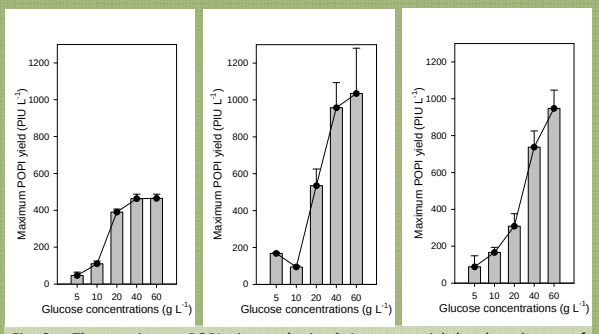


Fig 2 The maximum POPI titres obtained in sequential batch cultures of immobilized *Fusarium* sp. CMI397470 in response to glucose quantity supplied (a) Batch 1, (b) Batch 2, (c) Batch 3.

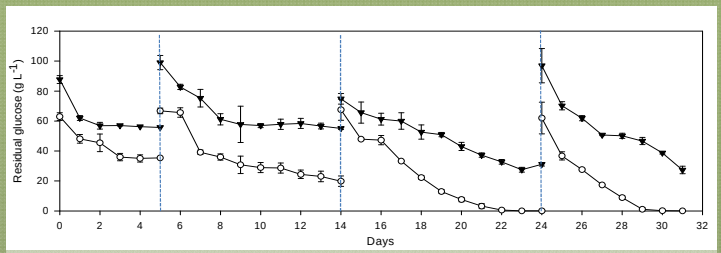


Fig 3 Glucose consumption by immobilized Fusarium sp. CMI397470 in Parker Glucose Broth in growth batch and 3 sequential POPI production batches.

References

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