TECHNOLOGY PROFILE

Clean Green Ephedrine Manufacturing Process

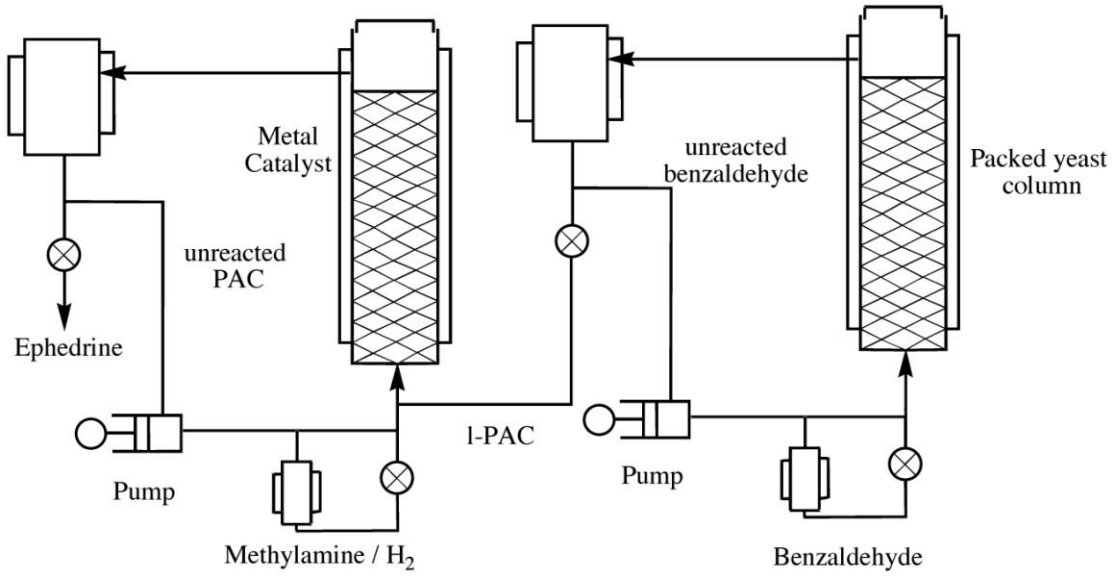
Technology Overview:
Researchers at Victoria University's School of Engineering and Science in the Faculty of Health, Engineering and Science, led by Associate Professor Andrew Smallridge and Associate Professor Maurice Trewhella, have developed an innovative two stage process for the manufacture of ephedrine using supercritical carbon dioxide. The process has potential application across a broad range of products. This patented technology uses less energy, produces less waste, and is expected to deliver substantial cost savings compared to existing manufacturing processes, thereby addressing many of the political and regulatory issues associated with reducing carbon emissions. A brief summary of the process is described below:

Stage 1

Benzaldehyde and pyruvic acid are condensed to form l-phenylacetylcarbinol (l-PAC) in supercritical carbon dioxide (SC-CO_2) through a column of solid bakers' yeast. Manipulation of temperature and pressure allows pure product to be separated from the reaction mixture and then passed to a second reactor.

Stage 2

In the second reactor SC-CO_2 is again employed as the medium, and l-PAC is reacted with hydrogen and methylamine over a metal catalyst to yield ephedrine. Manipulation of temperature and pressure enables pure ephedrine to be isolated.



State of Development:
Compared to traditional methods of manufacturing ephedrine, this patented process does not involve any fermentation: there is no requirement for large scale fermenters, sterile conditions, high-shear mixing or nutrient dosing. No organic solvents are required for isolation or purification of l-PAC or ephedrine.

In contrast with fermentation, which is a batch process that usually takes days to produce a single batch, the Victoria University process achieves high conversions in just a few hours and has the

potential to be continuous. The benzyl alcohol which is produced as an unwanted by-product of the first stage of the traditional process is all but eliminated in the Victoria University process with insignificant amounts being generated.

Stage 1 of the patented process has been proven at laboratory scale (100mg) and at pilot scale (200g) while Stage 2 has been proven at laboratory scale and can be readily scaled up.

Victoria University has a large range of supercritical fluid equipment including small-scale reactors and extractors, a supercritical NMR spectrometer, and access to a pilot plant facility. Our lead researchers each have more than twelve years experience working with supercritical systems.

Intellectual Property Position:
The process is protected by the following patents:

Methods for the Synthesis of Amines such as Ephedrine and Intermediates

2002328659	Australia	Granted
1421055	Europe	Granted
217174	India	Granted
7176332	United States	Granted

New Conditions for Reactions Mediated by Yeast

2004201110	Australia	Granted
2462063	Canada	Pending
7723065	United States	Granted

Yeast-Based Process for Production of l-PAC

2001021294	Australia	Granted
1240347	Europe	Granted
1409768	China	Granted
519329	New Zealand	Granted
7063969	United States	Granted

Yeast-Based Process for Production of l-PAC

6271008	United States	Granted

Market Overview:

The world market consumes approximately 1,500 to 2,000 tons of ephedrine products per annum, of which approximately half is produced by German companies using synthetic methods of manufacturing.

In China natural extraction methods are used to extract ephedrine from ephedra plants; however, there is a shift to synthetic manufacturing processes in order to reduce the destruction of grasslands being cleared to grow ephedra which is also used in traditional Chinese medicine.

Ephedrine is used in the pharmaceutical industry to produce drugs to treat allergy conditions, increase blood pressure, strengthen heart contractions, and to treat narcolepsy, depression and Myasthenia Gravis. Ephedrine is also used to assist weight loss but this application is prohibited in the United States.

Opportunities for Technology Co-development:
An opportunity exists for exclusive/non-exclusive licensing of the existing technology.

Opportunities also exist for investment and/or partnership agreements to further develop/expand the technology for other biotechnology applications.

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