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Purified Solutions

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Food & Beverages

Isolation of an antibiotic Oligopeptide

Polishing of an anticancer API

API: Anastrozole

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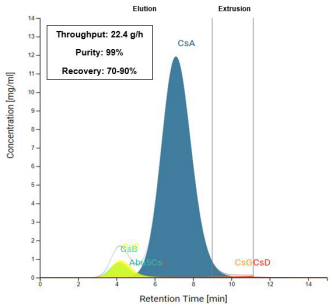
Active Pharmaceutical Ingredient(API)
Cyclosporine A (CsA)
Goal: Purification

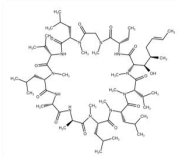
Cyclosporine A is a cyclic oligopeptide, with a lipid side-chain. It is produced by fermentation. The result of fermentation is usually a mixture of products with closely related structural properties. These are usually purified by classical purification methods: a combination of crystallization and preparative HPLC. To avoid costly two-step purification methods, RotaChrom developed a CPC solution which can produce pure Cyclosporin in 15 minutes on an industrial- scale.

API: Anastrozole
Goal: Polishing the API

Anastrozole is a pharmaceutically active agent, acting as a selective nonsteroidal aromatase inhibitor. Guidelines for API manufacturers mention that impurities must be kept below set limits. The study's goal was to replace a purification step which needed column chromatography. At the end of the study, RotaChrom's method could produce Anastrozole with higher than 99% purity, all in one step. After CPC purification, >99.9% purity can be achieved in a single crystallization step.

Isolation of an Antibiotic Oligopeptide

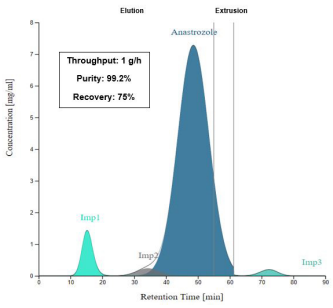


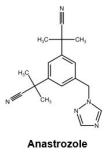


Cyclosporine A

Sample	Crude cyclosporine A
Apparatus	rCPC
Solvent system	Alkane-based solvent system
Flow rate	200 mL/min
Rotation	1000 rpm
Mode	Descending

Polishing of an Anticancer API





Anastrozole

Sample	Crude Anastrozole
Apparatus	labCPC
Solvent system	Ethereal solvent system
Flow rate	14 mL/min
Rotation	2000 rpm
Mode	Descending

Isolation of Mitragynine

Compound of Interest (CoI): Mitragynine

Goal: Isolation of the CoI
This compound is a major alkaloid in *Mitragyna speciosa* leaf extract. Closely related alkaloids are also present in the extract besides mitragynine. These include speciogynine (SG), speciociliatine (SC) and paynantheine (PM). CPC isolated mitragynine from samples cost-effectively with as high purity (99%) compared to other techniques. The developed method could purify directly from the crude extract.

Isolation of plasma proteins

CoI: Recombinant Human Albumin (rHA)

Goal: Isolation of the CoI
To this day, the Cohn method is the most widely used core fractionation technique. However, it comes with high initial investment and maintenance cost.

At the end of the study, the resulting rCPC method could isolate rHA with higher than 95% purity and high recovery.

In addition, the process needed fewer steps, and it turned out to be more economical than conventional solutions.

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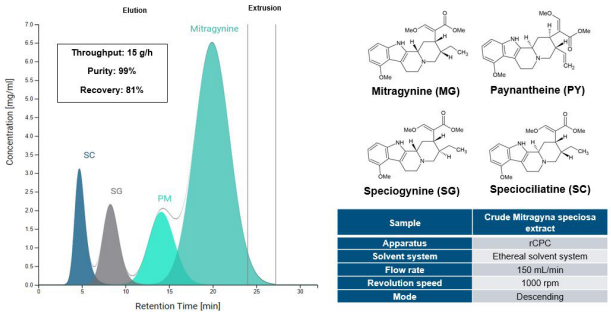
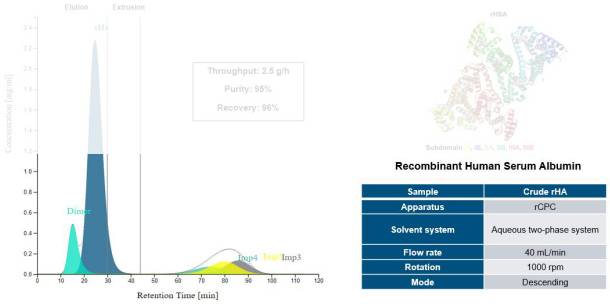
Isolation of Mitragynine



Sample	Crude Mitragyna speciosa extract
Apparatus	rCPC
Solvent system	Ethereal solvent system
Flow rate	150 mL/min
Revolution speed	1000 rpm
Mode	Descending

Isolation of a Plasma Protein



Sample	Crude rHA
Apparatus	rCPC
Solvent system	Aqueous two-phase system
Flow rate	40 mL/min
Rotation	1000 rpm
Mode	Descending

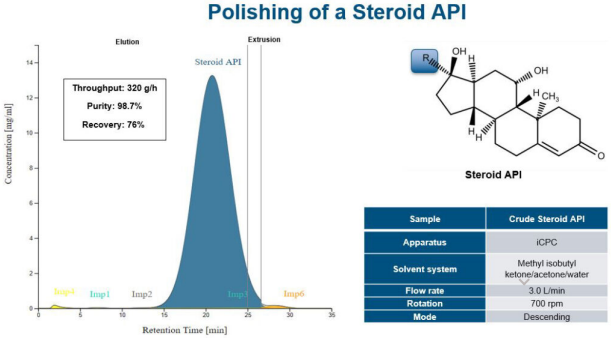
API

API: Steroid

Goal: Purification

A microbiological fermentation process produces this API. However, if reaction selectivity is compromised, stereoisomer of the API and other by-products appear in the process. Conventional production techniques of this API require steps that result in a significant loss of the yield. During the last step only, which is a preparative HPLC step, the loss is 70%. Using our CPC method, a yield of above 90% can be achieved with the similarly high purity. Because of the remarkable selectivity value, the system can be loaded well despite the low solubility of the API.

Polishing of a Steroid API



Sample	Crude Steroid API
Apparatus	iCPC
Solvent system	Methyl isobutyl ketone/acetone/water
Flow rate	3.0 L/min
Rotation	700 rpm
Mode	Descending

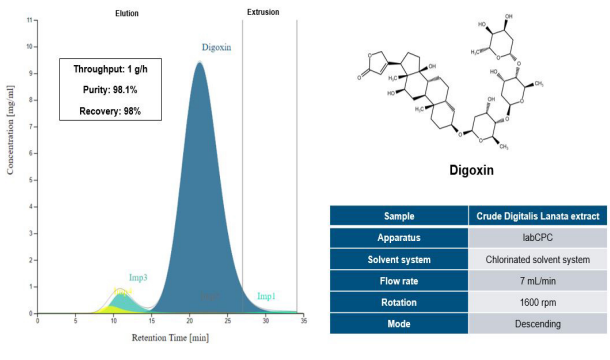
Isolation of Digoxin from a natural extract

Col: Digoxin. A secondary cardiotonic glycoside isolated from the fermented foliage of foxglove (*Digitalis lanata*).

Goal: Isolation

High-value bioactive compounds are usually surrounded by compounds of similar structure. These are often difficult to be isolated in their pure forms. Digoxin's mono- and bisdigitoxosides, digoxigenin and gitoxin were the main impurities that needed remediation. At the end of the study, we separated Digoxin directly from the crude extract.

Isolation of Digoxin from a natural extract



Sample	Crude Digitalis Lanata extract
Apparatus	labCPC
Solvent system	Chlorinated solvent system
Flow rate	7 mL/min
Rotation	1600 rpm
Mode	Descending

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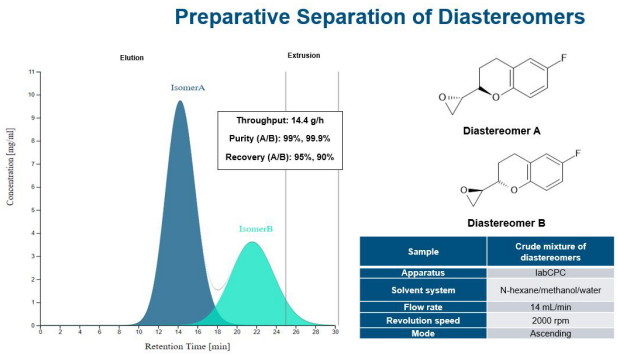
Preparative separation of diastereomers

Col: Benzopyrene compound

Goal: Separation

Diastereomers of an optically active substance are similar in structure, but show significant differences in pharmacodynamic properties. This benzopyrene compound is a precursor for a ß1 receptor blocker drug. The sample consisted of about 57% isomer A and 31% isomer B. We achieved high purity and recovery for both diastereomers. Running the rotor in ascending mode further encouraged the recovery of products.



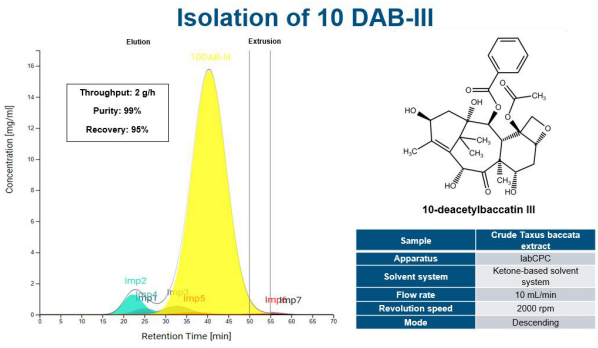
Sample	Crude mixture of diastereomers
Apparatus	labCPC
Solvent system	N-hexane/methanol/water
Flow rate	14 mL/min
Revolution speed	2000 rpm
Mode	Ascending

Isolation of 10 DAB-III

Col: 10 DAB-III from *Taxus baccata* extract.

Goal: Isolation

Docetaxol is a taxane diterpenoid, used as a chemotherapeutic drug. It is prepared from 10-DAB III by a semi-synthetic method. The crude extract contained a large amount of co-extractives along the taxanes of interest. Therefore, a purification step was needed to remove them. Our CPC method isolated 10 DAB-III with excellent purity and yield, and offered an efficient and cost-effective solution for purification on a large scale.



Sample	Crude Taxus baccata extract
Apparatus	labCPC
Solvent system	Ketone-based solvent system
Flow rate	10 mL/min
Revolution speed	2000 rpm
Mode	Descending

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Cosmetics & Fragrances

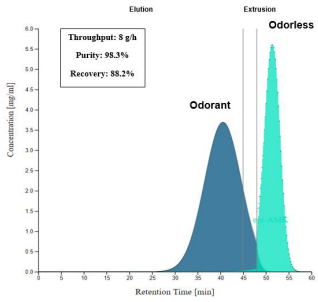
Preparative separation of epimer diterpenes

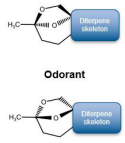
Goal: Separation of epimers
Ratio of epimers in the starting material:

7:3

The Compound of Interest is a synthetically produced perfume ingredient. It's important to note that this separation was yet to be solved cost-effectively by either column chromatography or fractional distillation. The selectivity value between the CoI and its epimer (1.59) in the selected solvent system is unprecedentedly high in the field of small molecule and chromatographic epimer separation. Selectivity of this scale typically requires chiral stationary phase,

Preparative separation of Epimer Diterpenes





Odorless

Sample	Crude Diterpene Mixture
Apparatus	rCPC
Solvent system	N-heptane/Acetone/Methyl tert-butyl ether/Nitromethane
Flow rate	150 mL/min
Rotation	1000 rpm
Mode	Descending

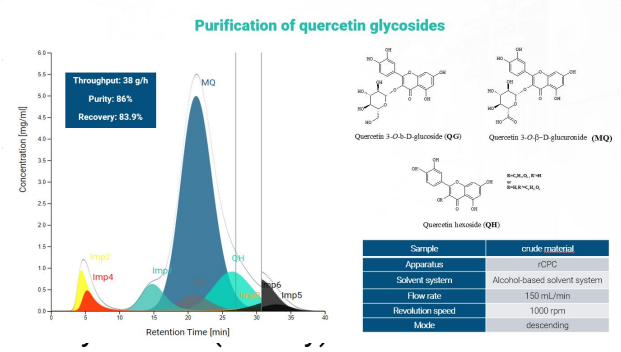
Preparative separation of ecdysteroids

Starting Material: Ecdysteroid-rich *Cyanotis arachnoidea* extracts
Goal: Isolation and purification

Separation of Vitamin E isomers

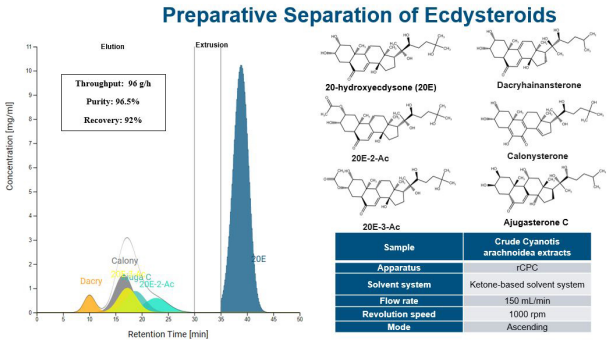
CoI: Tocotrienols and Tocopherols (members of the vitamin E family)

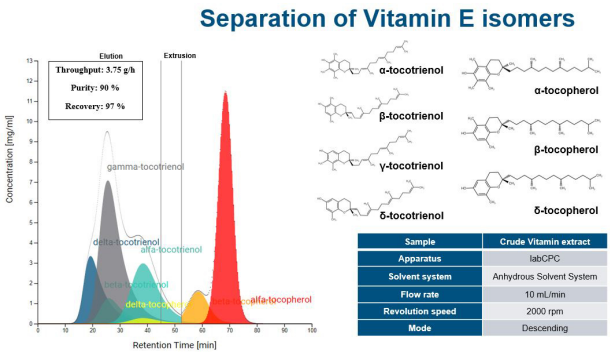
Goal: Separation
The oil included vitamin E isomers such as α-tocopherol, α-tocotrienol, β-tocopherol,



derivatives. Our CPC method At theAt the remarkable selectivity for 20E. This means our technology can isolate 20E with excellent purity and recovery.

β-tocotrienol, γ-tocotrienol, δ-tocopherol and δ-tocotrienol. Our CPC method could fractionate tcotrienols and tocopherols with excellent loading capacity: 50 ml injected volume to a 250 ml rotor. It achieved high selectivity for both the individual tocotrienols and tocopherols. The new method applied an anhydrous solvent system, which facilitated the recovery of the end product after the CPC run.



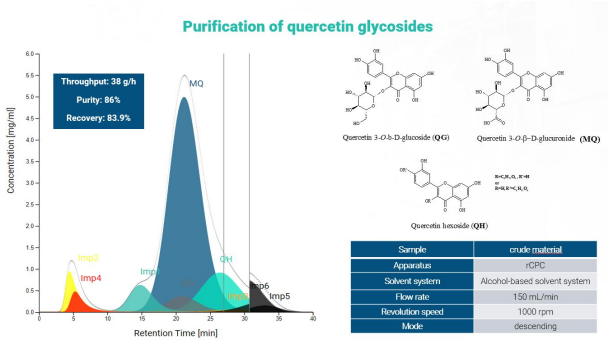


Purification of quercetin glycosides

Goal: Separation

The separation task was to investigate the feasibility of the isolation of quercetin glycosides. The primary objective was to achieve a purity value greater than 75% by weight for quercetin-3-β-O-D-glucoside (QG) quercetin-3-O-β-D-glucuronide (MQ) and a quercetin hexoside (QH) using food-grade solvents.

After extraction the developed CPC method was capable of isolating the three target compounds together with purity greater than the expected. It had a high throughput using only food grade chemicals. The end product could be re-crystallized from water which could further increase purity.



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