PuroSynth™

Resins for Solid Phase Peptide Synthesis

PuroSynth™ supports for Solid Phase Peptide Synthesis (SPPS) made of polystyrene crosslinked with 1% DVB, characterized by uniform particle size distribution, high swelling and excellent performances in peptide synthesis.

Purolite® Life Sciences

www.purolite.com/life-sciences

Why Purolite®?

For over 35 years, Purolite® has supplied specialty ion exchange resin technology to industries within complex regulatory environments, including biotechnology, pharmaceutical, food, fine chemical and electric power generation. Purolite® is the only global company to focus 100% on resin technology.

About Purolite® Life Sciences

Formed in 2012, Purolite® Life Sciences provides API's, enzyme carriers and immobilized enzymes, and resins for purification and separation, to support research and development and production-scale applications in pharmaceuticals, protein purification, food production, bioprocessing, fine chemical and other markets.

Purolite®'s team of world-class researchers and scientists develop novel, high-demand and customized products to meet customer needs.

Collaborating with industry organisations and research institutes all over the world, our aim is to produce the most economical and practical resin technology products available.

Purolite® has completed major refurbishments and the expansion of its Life Sciences research laboratories located in Llantrisant, South Wales UK, including the addition of a world scale agarose manufacturing plant.

Essential to life science, we are employing global quality and regulatory management systems and a team of experts to ensure the highest product quality.

Purolite® has a FDA inspected facility located in Romania, which has recently completed a fourth cleanroom addition. This adds to our speciality polymer capabilities with separate facilities to immobilize enzymes or ligands, backwash towers for the removal of fines, solvent or purified water washing, screening, vacuum drying and packaging. All processes are completed in a cleanroom environment with gowning and trained personnel.

In addition, Purolite® is continuing its expansion in Romania with two polymer reactors located in a separate cleanroom environment for the production of various types of specialty polymers. The addition, provides Purolite® with the capabilities to manufacture products through suspension polymerization, or through our patented uniform bead jetting process.

Once the products are manufactured they are functionalized, washed and packaged as required.

These expansions and additional facilities are a result of increased demand for large scale production of polymer beads ranging between 25 – 250 µm in size. This unique capability, means that commercial production can now take place on a large scale, producing beads of varying size in a short period of time.

Purolite® is a solutions company; we work with you to assist in taking your ideas and processes forward, to commercialize them.

Product Portfolio

Chromalite® Synthetic Resins

- Robust styrene/DVB resins and methacrylic resins with excellent pH and chemical stability
- Excellent pressure and flow characteristics
- Ideal for the separation of biomolecules such as proteins, amino acids, peptides & oligonucleotides

PuroPhase™ SPE Reverse Phase

- Wide range of Chromalite synthetic adsorbents packed in SPE columns
- Different adsorbents with a range hydrophobicity/ hydrophilicity and chemical/physical properties
- Ideal for Solid Phase Extraction (SPE) of different analytes

Praesto® Agarose Resins

- Advanced high-flow, highly cross-linked agarose
- Excellent performance with chemical and physical stability
- The best Protein A and ion-exchange resins for biological protein chromatography

Lifetech™ Enzyme Carriers & Immobilized Enzymes

- Wide range of methacrylic or styrenic copolymers for immobilization of different enzymes and ready-to-use industrial immobilized lipases
- Superior physical, chemical and mechanical stability to allow multiple cycles
- Ideal for column or batch reactor design

PuroSynth™ for Solid-Phase Peptide Synthesis (SPPS)

- Available as Merrifield, Wang, 2-chlorotrityl, MBHA and aminomethyl functionalise resins
- Uniform particle size for better kinetics and purity of final peptide
- High swelling

Pharmaceutical APIs & Excipients - Purolite®

- Wide range of functionalized synthetic acrylic or styrene resins
- Manufactured to meet the requirements of both the US Food and Drug Administration (FDA) and the European Union
- Used for a range of pharmaceutical applications including reducing the blood cholesterol levels, hyperkalemia and taste/odour control

Chromalite® Purophase™

Synthetic Resins

Praesto®

Agarose Resins

Purolite® Life Sciences

Lifetech™

Enzyme Carriers and Immobilized Enzymes

PuroSynth™

Solid Phase Peptide Synthesis

100% focused on synthetic resin technology.

A solutions company, working hand-in-hand with our customers.

25+ years of regulatory experience from FDA inspected cGMP facility.

Over 35+ years of experience in solving advanced industrial challenges.

Leading innovation. Exceeding expectations.

Contents

PuroSynth™ - Resins for Solid Phase Peptide Synthesis

Background

Polystyrene is the most common core resin used in solid phase peptide chemistry, due to its chemical stability, compatibility with the majority of organic solvents, and of course cost and availability.

PuroSynth™ supports for Solid Phase Peptide Synthesis (SPPS) are made of polystyrene containing 1% divinylbenzene (DVB) as a crosslinking agent. This polystyrene resin is insoluble in all common solvents, it swells well in most organic solvents and is supplied as uniform spherical beads.

Key Advantages

The key advantages of PuroSynth™ resin for Solid Phase Peptide Synthesis include:

- Complete range of products for Fmoc[1] and Boc[2] chemistry
- Narrow particle size distribution (manufactured by jetting)
- Large scale batches (500+ Kg per batch)
- Performances equivalent to, or better than, main products
- Controlled residual organics in the resins, leading to higher purity of final peptide
- Made in the EU in an ISO 9001:2008 and ISO 18001:2007 certified facility

[1] Fmoc: 9-fluorenylmethyloxycarbonyl

[2] Boc: tert-butyloxycarbonyl

PuroSynth™ - Product Line

As shown in both Figure 1 and Table 1, PuroSynth™ resins for Solid Phase Peptide Synthesis are offered with 5 different functionalities:

- PuroSynth™ CM
- PuroSynth™ Wang
- PuroSynth™ CTC
- PuroSynth™ MBHA
- PuroSynth™ AM

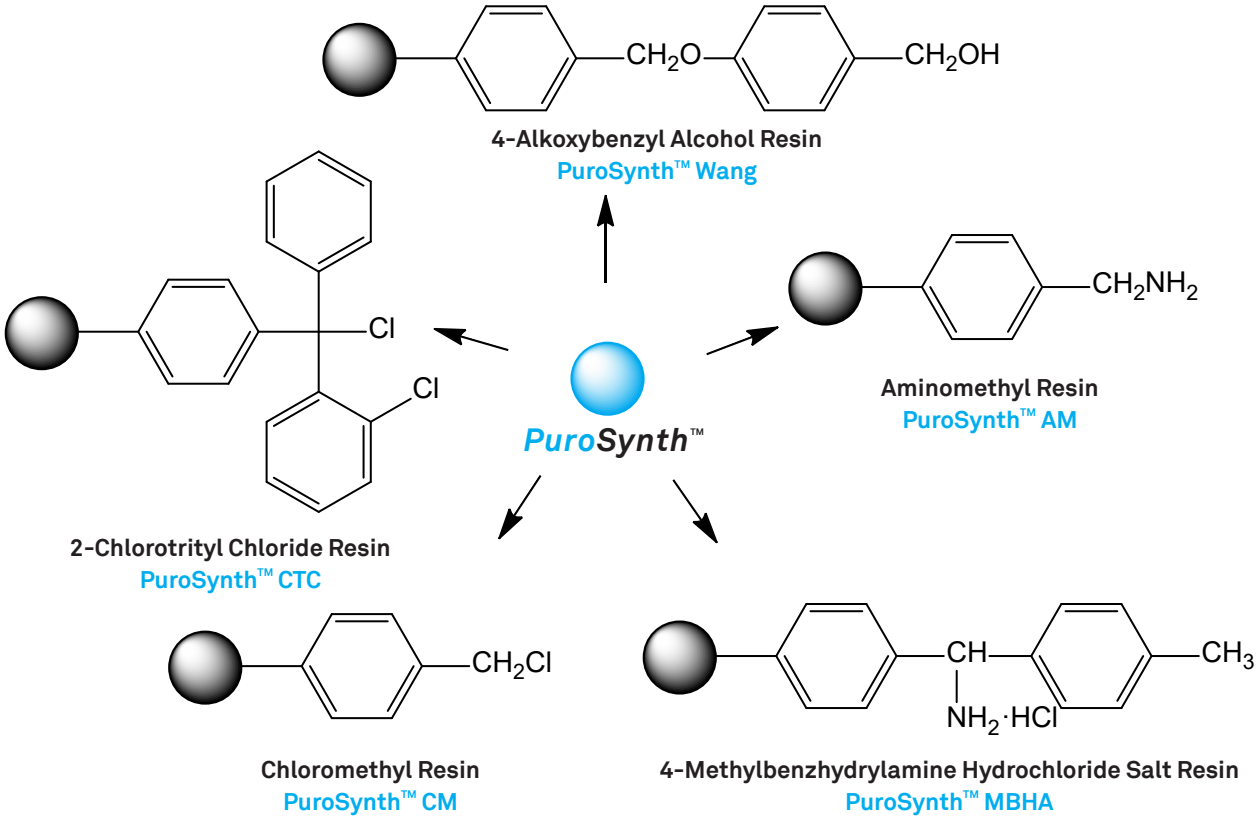


Figure 1. Chemical structures of PuroSynth™ *product range*

Key Features of PuroSynth™ Product Range

Product	Functional Group	Particle Size Micron (USA Mesh)[a]	Loading (mmol/g)[b]	Description
PuroSynth™ CM/S	**C**hloro**m**ethyl Resin	75 - 150 (100 - 200)	From 0.4 up to 1.6	PuroSynth™ CM (Merrifield resin) is the standard support for the acid peptide synthesis by Boc strategy. The first amino acid is attached to Merrifield resins by nucleophilic displacement of chlorine. The resulting resin-substrate bond is stable in mild acids such as trifluoroacetic acid (TFA) and requires strong acid conditions for cleavage such as HF.
PuroSynth™ Wang/S	4-Alkoxybenzyl Alcohol Resin (**Wang** linker)	75 - 150 (100 - 200)	From 0.4 up to 1.2	PuroSynth™ Wang (4-Alkoxybenzyl alcohol resin) is the standard support for acid peptide synthesis by Fmoc strategy. The linkage between the first amino acid and the support has good stability to a variety of reaction conditions, but can be readily cleaved by moderate treatment with an acid, such as TFA.
PuroSynth™ CTC/S	2-**C**hloro**t**rityl **C**hloride Resin (2-CTC Resin)	75 - 150 (100 - 200)	From 0.4 up to 1.2	PuroSynth™ CTC (2-chlorotrityl chloride resin) is very acid labile, and peptide can be cleaved with a very low concentration of TFA and even with hexafluoroisopropanol. The first amino acid is easily incorporated to the resin by chlorine displacement. Although, it can be used for the preparation of unprotected peptides, this resin is particularly useful for the preparation of protected peptides by Fmoc strategy.
PuroSynth™ MBHA/S	4-**M**ethyl**b**enz**h**-dryl**a**mine Hydrochloride Salt Resin (MBHA Resin)	75 - 150 (100 - 200)	From 0.4 up to 1.2	PuroSynth™ MBHA (4-methylbenzhydrylamine resin) is used in the synthesis of amide peptides by Boc strategy. The method used to attach the first amino acid is ordinary amide bond forming conditions. For cleaving peptide products from MBHA the concourse of HF or trifluoromethanesulfonic acid (TFMSA) is required. It can also be used as a base for the incorporation of a great variety of linkers such as the Fmoc-Rink amide linker.
PuroSynth™ AM/S	**A**mino**m**ethyl Resin	75 - 150 (100 - 200)	From 0.4 up to 1.2	PuroSynth™ AM (aminomethyl resin) is the core resin to which various linkers could be attached through a stable amide bond. Particularly, the incorporation of the Fmoc-Rink amide linker renders the resin optimal for the preparation of amide peptides by a Fmoc based strategy.

[a] S grade : 75 -150 micron (100-200 mesh); F grade : 40 - 75 micron (200-400 mesh) available on request.

[b] Available in 6 different loadings : 0.4-0.6, 0.6-0.8, 0.8-1.0, 1.0-1.2, 1.2-1.4, 1.4-1.6 mmol/g.

Table 1. Key Features of PuroSynth™ product range

General Features of PuroSynth™ Resins

DESCRIPTION	CHARACTERISTIC
Resin	Polystyrene
Cross-linking	1% Divinylbenzene (DVB)
Supplied as	Dry
Loss on drying (%)	≤2
Chemical resistance	Stable to all organic solvents and chemicals
Temperature resistance	Up to 140 °C
Swelling (ml/g)	Up to 9 ml/g
Particle size range (micron)	75 – 150 (S grade) 40 -75 (F grade)
Particle size range (mesh)	100 - 200 (S grade) 200 - 400 (F grade)
Uniformity coefficient (UC)[1]	< 1.3
Typical loading (mmol/g)	0.4-0.6; 0.6-0.8; 0.8-1.0; 1.0-1.2; 1.2-1.4; 1.4-1.6
Optimal storage conditions	2 – 20 °C
Packaging	• Heat-seal, PP bottle • Aluminium bags in kegs
Typical industrial batch	500+ Kg per batch
Typical packaging options	25g, 100g, 1Kg, 5Kg and 20Kg
Expiry date	1 year

[1]The uniformity coefficient is defined as: UC = d60/ d10. This coefficient measures the "width" of the distribution, and is reflected in the width of the Gaussian bell curve. If all beads had the same size, it would be equal to 1.0.

Table 2. General Features of PuroSynth™ *product range*

Swelling Properties of PuroSynth™ Resins

Even though the cross-linked polystyrene of PuroSynth™ resin is insoluble in organic solvents, it swells in aprotic solvents such as dimethylformamide (DMF), dichloromethane (DCM), acetonitrile (ACN) and the green solvents 2-methyltetrahydrofuran (MeTHF) and γ-valerolactone (GVL) as shown in Figure 2.

The advantage of having a 1% DVB cross-linked resin is that it results in a significant increase in swelling, compared to a higher cross-linked resin as a polystyrene with 2% DVB.

Resin swelling is a key factor in solid phase peptide synthesis, since reaction kinetics are diffusion controlled. Consequently, a resin that swells more will have a higher diffusion rate of reagents into the core of the matrix, resulting in shorter reaction times and more complete chemical conversions.

The good solvent properties of PuroSynth™ resins in green solvents, such as MeTHF and biomass derived GVL open up the possibility to use these resins on green chemistry processes for green solid phase peptide synthesis.

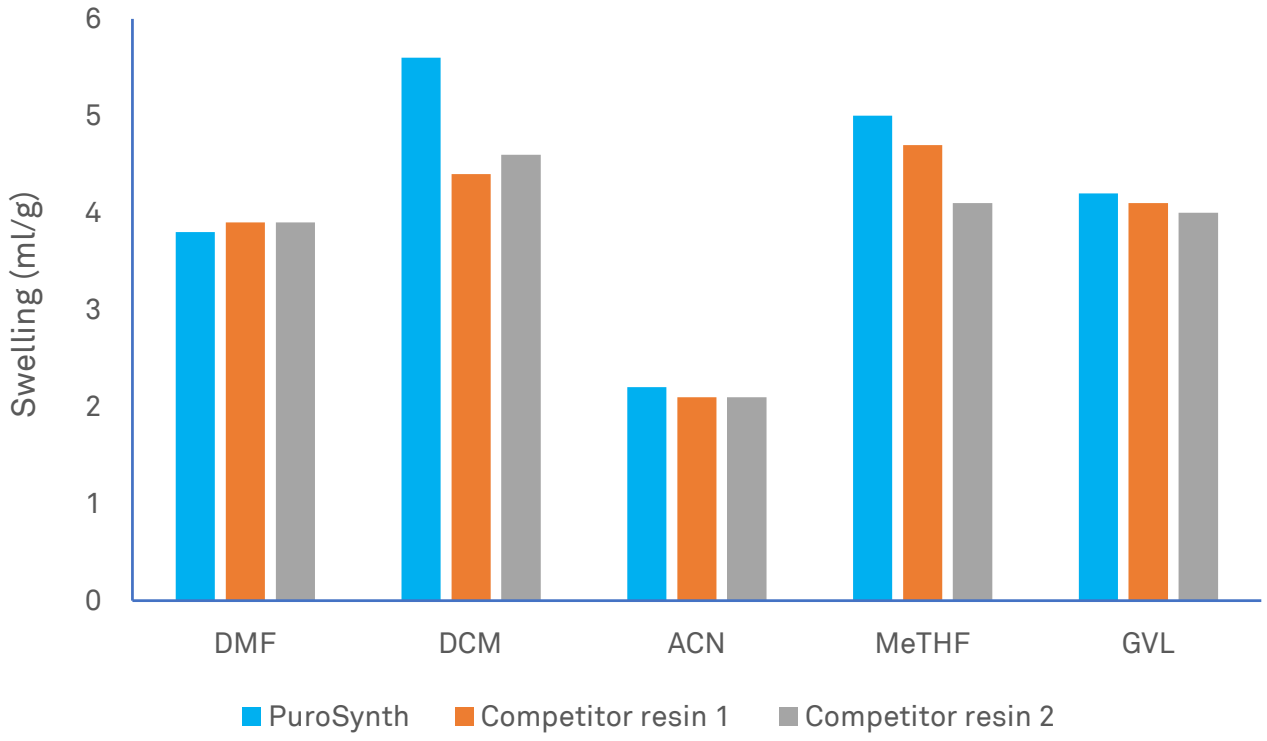


Figure 2. The swelling properties of PuroSynth™

Particle Size Distribution of PuroSynth™ Resins

Particle Size Distribution

One of the key features of PuroSynth™ products is the narrow particle size distribution due to the unique manufacturing process. 'Jetting' - the Purolite® patented manufacturing process, allows the production of uniform particle size, with low uniformity coefficient and high productivity in a continuous mode. This enables a more economic and environmentally friendly (reduced waste) process, than classic batch emulsion polymerisation.

The narrow particle size distribution obtained by jetting does not require further screening as is the case in competing products for SPPS. Jetting technology allows the production of large batches (500+ kg) in a very short time. In SPPS, the uniformity of particle size offers great advantages in terms of uniform kinetics and swelling during peptide synthesis, and so ensures better purity of the final peptide.

PuroSynth™ products are manufactured using membrane or 'can' jetting (Figure 3), which uses a membrane with very small, discrete orifices, through which the polymer is passed. This device is capable of producing uniform particle size resins from ~15 to 250 micron.

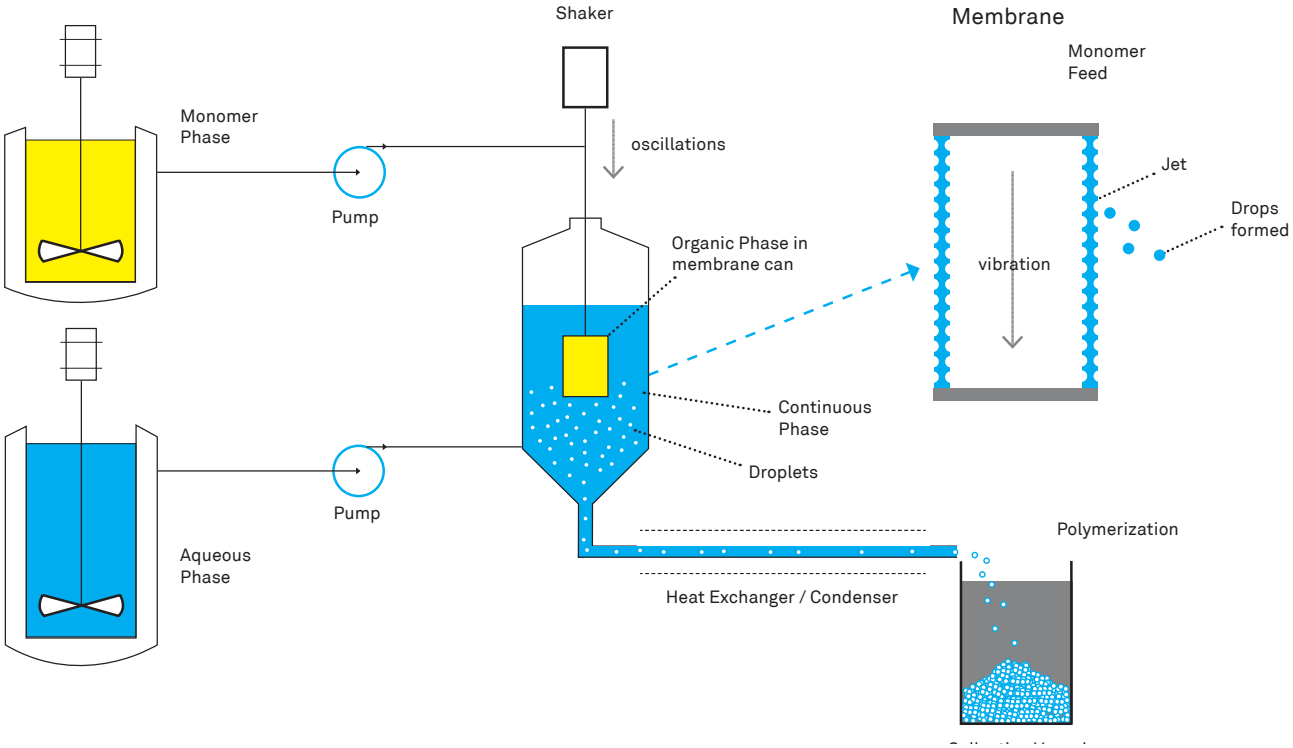


Figure 3. Jetting technology through a membrane for the manufacture of PuroSynth™ products.

Jetting Technology

The result of this jetting process is a narrow gaussian distribution of uniform spherical beads. Figure 4 shows an example of a particle size distribution of PuroSynth™ products. Figure 5 shows an electron microscopy picture for PuroSynth™ products.

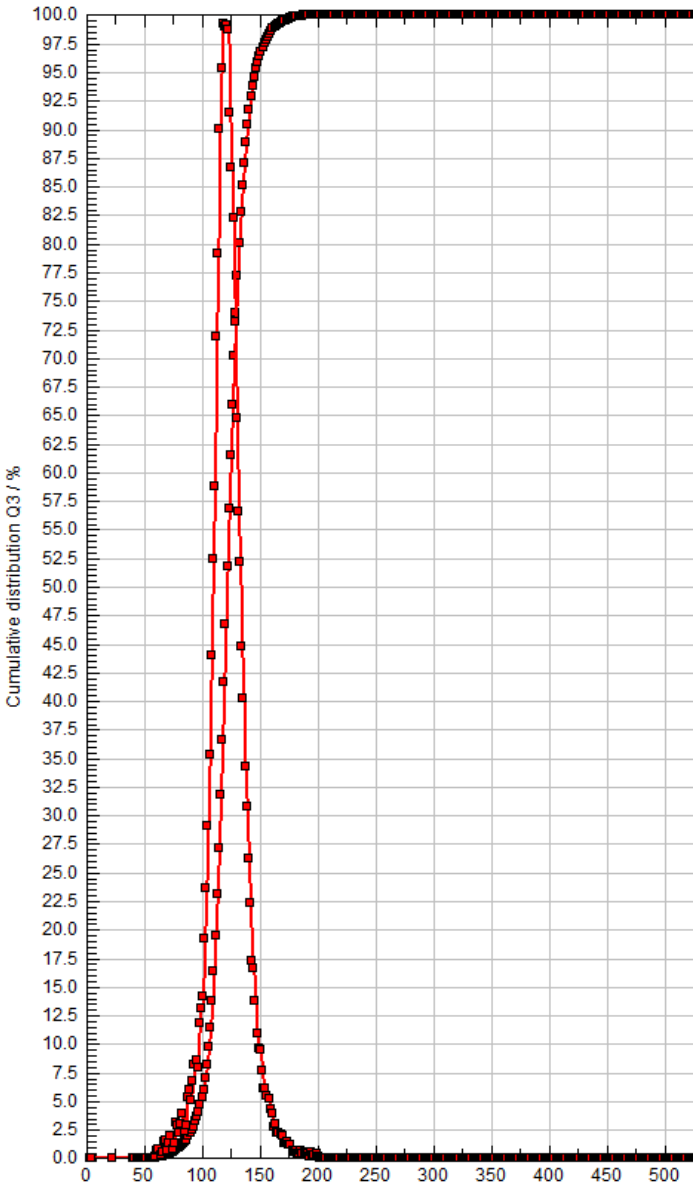


Figure 4. Particle size distribution for a batch of PuroSynth™ *CTC/S with UC 1.2.*

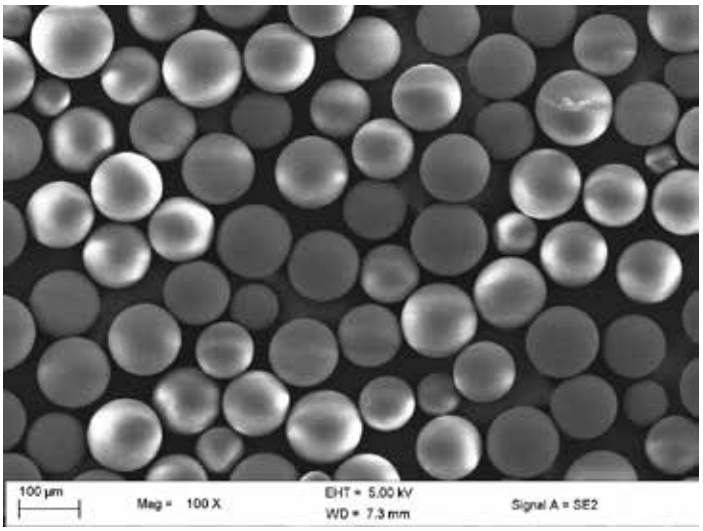


Figure 5. Electron microscopy images for PuroSynth™ *Wang/S*

PuroSynth™ - Applications

PuroSynth™ resins have been tested by Prof. Fernando Albericio in the University of KwaZulu-Natal, School of Chemistry, Durban (South Africa) and in the University of Barcelona, Department of Organic Chemistry, Barcelona (Spain).

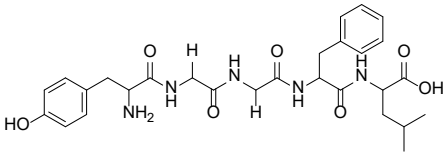
Performances have been evaluated in terms of the purity of the final product and recovery. Synthesis of model peptides has been carried out in both automatic assisted heating microwave systems and in manual mode.

Standard SPPS conditions used are Fmoc/tButyl chemistry and DIC-OxymaPure for coupling; 20% piperidine/DMF for Fmoc removal in DMF as a solvent.

Results show that PuroSynth™ resins are efficient in the synthesis of peptides ranging from 5-mer (Figure 6) up to 28-mer (Figure 10). In all cases PuroSynth™ functionalized resins provide excellent purity (measured by HPLC) and recovery of final peptide (determined by weight increase) also, when compared to commercially available products.

Synthesis of a pentapeptide (5 amino acids)

H-Tyr-Gly-Gly-Phe-Leu-OH



Chemical Formula: $C_{28}H_{37}N_5O_7$
Exact Mass: 555,27
Molecular Weight: 555,62

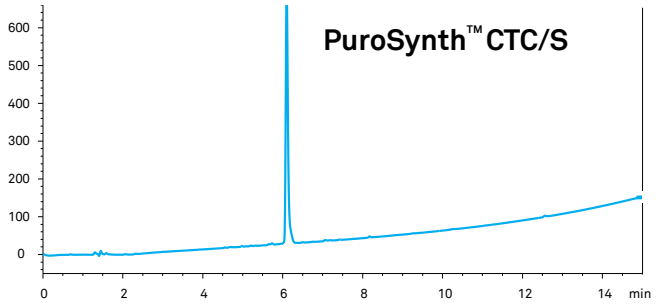
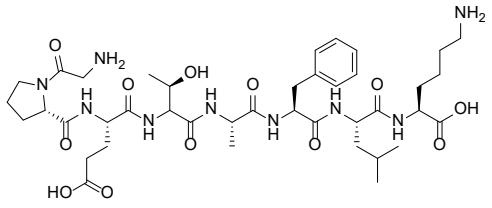


Figure 6. Synthesis of 5-mer peptide on PuroSynth™ CTC/S.

Synthesis of an octapeptide (8 amino acids)

H-Gly-Pro-Glu-Thr-Ala-Phe-Leu-Lys-OH



Chemical Formula: $C_{40}H_{63}N_9O_{12}$
Exact Mass: 861,46
Molecular Weight: 862,00

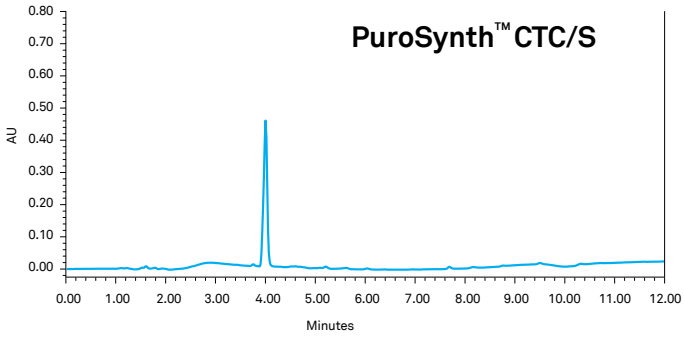


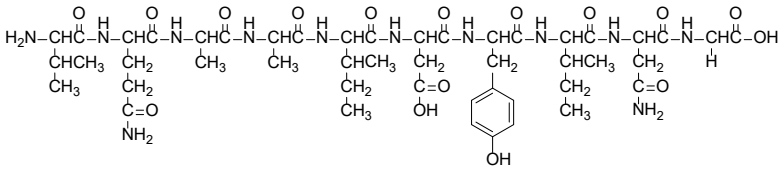
Figure 7. Synthesis of 8-mer peptide on PuroSynth™ CTC/S.

The above acid octapeptide was synthetised with similar purity and recovery using the PuroSynth™ CTC/S and the PuroSynth™ Wang/S resins. The amide version of this octapeptide was successfully synthetised using the PuroSynth™ AM/S containing the Rink linker resin.

Synthesis of ACP(65-74) peptide (10 amino acids)

ACP(65-74) is the current model peptide used to set up synthetic strategies.

H-Val-Gln-Ala-Ala-Ile-Asp-Tyr-Ile-Asn-Gly-OH



Chemical Formula: $C_{47}H_{74}N_{12}O_{16}$
Exact Mass: 1062,53
Molecular Weight: 1063,16

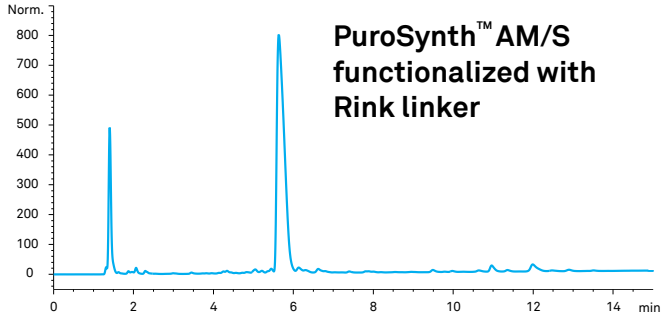


Figure 8a. Synthesis of 10-mer peptide on PuroSynth™ *AM/S*

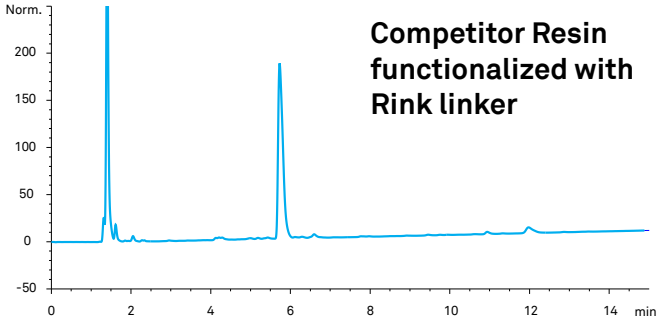
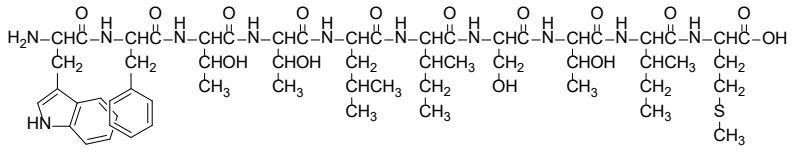


Figure 8b. Comparison with competitor AM resin.

Synthesis of Jung-Redemann decapeptide (10 amino acids)

Jung-Redemann decapeptide (JR) is the C-terminal part of a 26-mer peptide, considered a difficult sequence, more difficult to manufacture than ACP.

H-Trp-Phe-Thr-Thr-Leu-Ile-Ser-Thr-Ile-Met-OH



Chemical Formula: $C_{58}H_{89}N_{11}O_{15}S$
Exact Mass: 1211,63
Molecular Weight: 1212,46

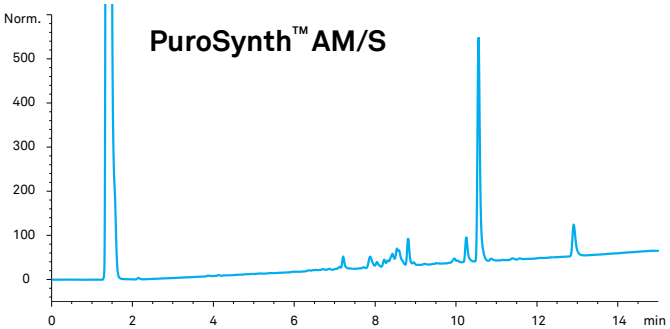


Figure 9a. Synthesis of 10-mer peptide on PuroSynth™ *AM/S*

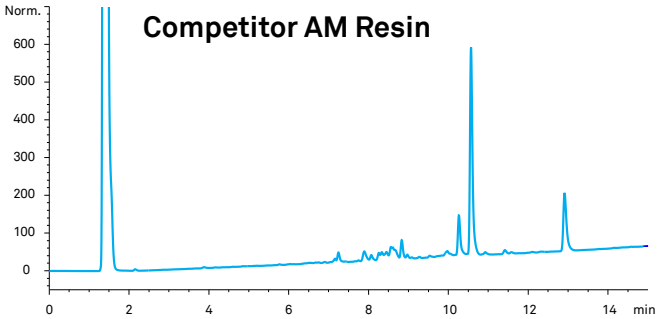


Figure 9b. Comparison with competitor AM resin

Synthesis of Thymosin peptide (28 amino acids)

Thymosin is a commercial product on the market.

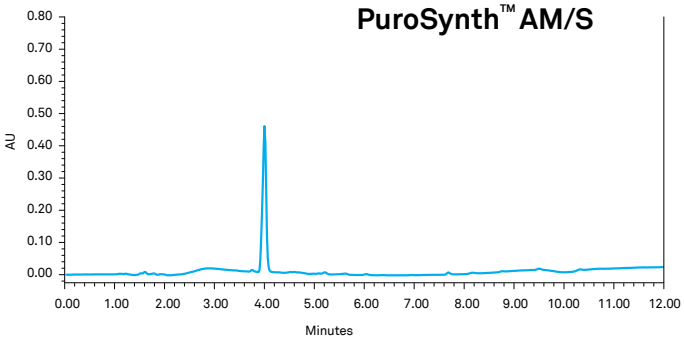
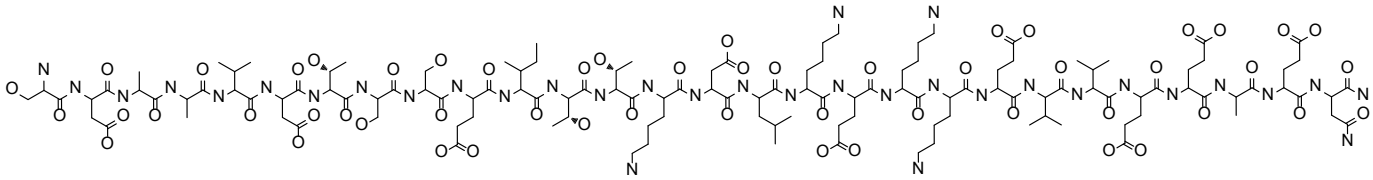


Figure 10. Synthesis of 28-mer peptide on PuroSynth™ *AM/S.*

H-Ser-Asp-Ala-Ala-Val-Asp-Thr-Ser-Ser-Glu-Ile-Thr-Thr-Lys-Asp-Leu-Lys-Glu-Lys-Lys-Glu-Val-Val-Glu-Glu-Ala-Glu-Asn-NH2



Chemical Formula: $C_{127}H_{214}N_{34}O_{53}$
Exact Mass: 3063,51
Molecular Weight: 3065,25

PuroSynth™ - Regulatory

All PuroSynth™ products are made in Europe under an ISO 9001:2008 and ISO 18001:2007 certified facility.

Ordering Information

Ordering Information

To place your order, simply contact the relevant regional office via email or telephone using the information on the back page of this brochure, and quote your order number from the tables on the following pages.

PuroSynth™ – Resins for Solid Phase Peptide Synthesis™		
PRODUCT	LOADING (mmol/g)	ORDER NUMBER
PuroSynth™ Wang/S	0.4 - 0.6	LSPS02001
	0.6 - 0.8	LSPS02011
	0.8 - 1.0	LSPS02021
	1.0 - 1.2	LSPS02031
PuroSynth™ CTC/S	0.4 - 0.6	LSPS03001
	0.6 - 0.8	LSPS03011
	0.8 - 1.0	LSPS03021
	1.0 - 1.2	LSPS03031
PuroSynth™ AM/S	0.4 - 0.6	LSPS04001
	0.6 - 0.8	LSPS04011
	0.8 - 1.0	LSPS04021
	1.0 - 1.2	LSPS04031
PuroSynth™ MBHA/S	0.4 - 0.6	LSPS05001
	0.6 - 0.8	LSPS05011
	0.8 - 1.0	LSPS05021
	1.0 - 1.2	LSPS05031
PuroSynth™ CM/S	0.4 - 0.6	LSPS01001
	0.6 - 0.8	LSPS01011
	0.8 - 1.0	LSPS01021
	1.0 - 1.2	LSPS01031
	1.2 - 1.4	LSPS01041
	1.4 - 1.6	LSPS01051

Packaging Codes	
QUANTITY	CODE SUFFIX
25 g	-163
100 g	-164
1 kg	-144
5 kg	-343
20 kg	-700

F grade resins available on request

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Purolite Life Sciences brings Purolite's innovative thinking and distinguished history of resin technology expertise to the global Life Sciences marketplace.

Over three decades, Purolite has grown into the world's premier resin technology manufacturer and innovation leader, with production plants and advanced research labs across the globe.

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