

Dipeptides make media preparation easier



Dipeptides have several advantages over the individual amino acids as components of chemically defined media, and address several challenges associated with using the corresponding individual amino acids.

The improvements to media stability and solubility gained by using dipeptides in cell culture media may lead to increases in viable cell density and/or product titer of the biopharmaceutical product. This is, of course, dependent on the particular cell line used.

In addition to our standard products, we can design and manufacture almost any dipeptide – please discuss your requirements with us.

Naturally, all our dipeptides are:

- Non-animal origin compounds
- cGMP compliant
- Consistent high purity chemical grades
- Microbiologically controlled with a low endotoxin level



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Evonik. Power to create.

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Evonik's Dipeptides:
Ingredients for Chemically
Defined Media

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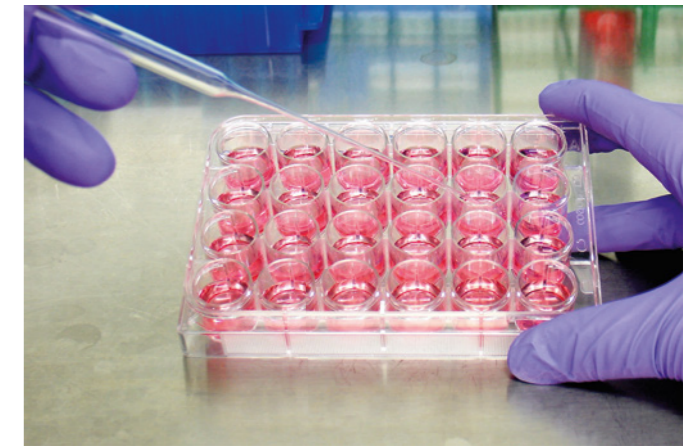
Cell culture media

The successful manufacture of biopharmaceuticals using mammalian cell cultures requires specialized cell culture media.

In the past, key media ingredients have been animal derived sera (such as fetal bovine serum) or undefined protein hydrolysates. Concern over potential contamination of animal derived components has led to their replacement by non-animal derived and chemically defined ingredients.

The importance of single chemically defined products as additives for culture media has been emphasized. Specific additives include metal salts, carboxylic acids, keto-acids and amino acids.

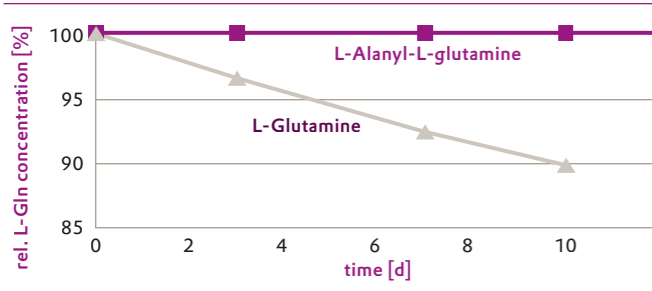
In addition to this, Evonik now offers also a range of dipeptides which overcome existing limitations.



Improvement in stability

L-Glutamine has limited stability in aqueous solution at pH 7. Dipeptides with C-terminal L-glutamine have been used to improve stability, particularly glycyl-L-glutamine and L-alanyl-L-glutamine.

Comparison of stability of aqueous solutions of L-glutamine and L-alanyl-L-glutamine

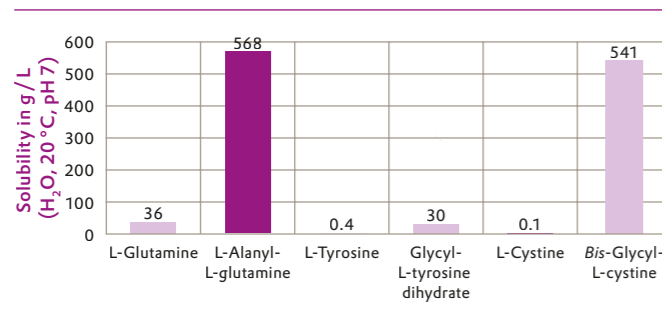


Stability of an aqueous solution (10 g/L) at 37 °C and pH 7

Improvement in solubility

L-Tyrosine and L-cysteine are particularly difficult to incorporate into cell culture media because of their low water solubility. Dipeptides of these two amino acids with an amino acid having a high water solubility (for example glycine) can be used to solve the problem.

Comparison of solubility for single amino acids and corresponding dipeptides



Glycyl-L-glutamine monohydrate: 154 g/l
N-Acetyl-L-alanyl-L-glutamine: > 500 g/l

P. Fuerst, *J. Nutrition*, 2001, 131, 2562

Availability of dipeptides for cell culture

N-Terminus	C-Terminus																				
	Ala A	Cys ¹ C	Asp D	Glu E	Phe F	Gly G	His H	Ile I	Lys K	Leu L	Met M	Asn N	Pro P	Gln Q	Arg R	Ser S	Thr T	Val V	Trp W	Tyr Y	Hse Hse
Ala	AA	AC	AD	AE	AF	AG	AH	AI	AK	AL	AM	AN	AP	AQ ²	AR	AS	AT	AV	AW	AY	AHse
Cys ¹	CA	CC	CD	CE	CF	CG	CH	CI	CK	CL	CM	CN	CP	CQ	CR	CS	CT	CV	CW	CY	CHse
Asp	DA	DC	DD	DE	DF	DG	DH	DI	DK	DL	DM	DN	DP	DQ	DR	DS	DT	DV	DW	DY	DHse
Glu	EA	EC	ED	EE	EF	EG	EH	EI	EK	EL	EM	EN	EP	EQ	ER	ES	ET	EV	EW	EY	EHse
Phe	FA	FC	FD	FE	FF	FG	FH	FI	FK	FL	FM	FN	FP	FQ	FR	FS	FT	FV	FW	FY	FHse
Gly	GA	GC	GD	GE	GF	GG	GH	GI	GK	GL	GM	GN	GP	GQ ²	GR	GS	GT	GV	GW	GY	GHse
His	HA	HC	HD	HE	HF	HG	HH	HI	HK	HL	HM	HN	HP	HQ	HR	HS	HAT	HV	HW	HY	HHse
Ile	IA	IC	ID	IE	IF	IG	IH	II	IK	IL	IM	IN	IP	IQ	IR	IS	IT	IV	IW	IY	IHse
Lys	KA	KC	KD	KE	KF	KG	KH	KI	KK	KL	KM	KN	KP	KQ	KR	KS	KT	KV	KW	KY	KHse
Leu	LA	LC	LD	LE	LF	LG	LH	LI	LK	LL	LM	LN	LP	LQ	LR	LS	LT	LV	LW	LY	LHse
Met	MA	MC	MD	ME	MF	MG	MH	MI	MK	ML	MM ⁴	MN	MP	MQ	MR	MS	MT	MV	MW	MY	MHse
Asn	NA	NC	ND	NE	NF	NG	NH	NI	NK	NL	NM	NN	NP	NQ	NR	NS	NT	NV	NW	NY	NHse
Pro	PA	PC	PD	PE	PF	PG	PH	PI	PK	PL	PM	PN	PP	PQ	PR	PS	PT	PV	PW	PY	PHse
Gln	QA	QC	QD	QE	QF	QG	QH	QI	QK	QL	QM	QN	QP	QQ	QR	QS	QT	QV	QW	QY	QHse
Arg	RA	RC	RD	RE	RF	RG	RH	RI	RK	RL	RM	RN	RP	RQ	RR	RS	RT	RV	RW	RY	RHse
Ser	SA	SC	SD	SE	SF	SG	SH	SI	SK	SL	SM	SN	SP	SQ	SR	SS	ST	SV	SW	SY	SHse
Thr	TA	TC	TD	TE	TF	TG	TH	TI	TK	TL	TM	TN	TP	TQ	TR	TS	TT	TV	TW	TY	THse
Val	VA	VC	VD	VE	VF	VG	VH	VI	VK	VL	VM	VN	VP	VQ	VR	VS	VT	VV	VW	VY	VHse
Trp	WA	WC	WD	WE	WF	WG	WH	WI	WK	WL	WM	WN	WP	WQ	WR	WS	WT	WV	WW	WY	WHse
Tyr	YA	YC	YD	YE	YF	YG	YH ³	YI	YK ³	YL	YM	YN	YP	YQ	YR	YS	YT	YV	YW	YY	YHse
Hse	HseA	HseC	HseD	HseE	HseF	HseG	HseH	HseI	HseK	HseL	HseM	HseN	HseP	HseQ	HseR	HseS	HseT	HseV	HseW	HseY	HseHse

■ Commercially available ■ Samples available

¹ Cysteine-containing dipeptides are usually provided as the S-S bridged cystine dimer. Please contact us to discuss supply of the free cysteine dipeptide.

² A. Christie, M. Butler, *J. Biotechnol.* 1994, 37, 277 (stability enhancement)

³ S. Kang et al, *Biotech. Bioeng.* 2012, 109, 2286 (solubility enhancement)

⁴ Y. Pan, K. Webb, *J. Nutr.* 1998, 128, 251