高等学校化学学报 2009, 30(7) 1410-1416 DOI: ISSN: 0251-0790 CN: 22-1131/O6

论文

PEG在线定点修饰水蛭素及其修饰位点的理论预测与分析

赵军, 李雪芹, 修志龙

大连理工大学环境与生命学院生物科学与工程系, 大连 116024

摘要:

比较了液相和固相修饰水蛭素的实验结果, 并在实验的基础上对水蛭素以及水蛭素/凝血酶复合物进行分子动力学模拟, 分析了容易被修饰的水蛭素赖氨酸残基的位点. 结果表明, 在液相修饰的时候, 水蛭素在水溶液中可被修饰的赖氨酸残基除Lys47外, 都容易被修饰. 而在固相修饰的时候, 水蛭素仅Lys35和Lys27容易被修饰.

关键词: 水蛭素; 分子动力学模拟; 聚乙二醇(PEG)修饰; 溶液可及表面积

Specific-site PEGylation of Hirudin on Ion-exchange Column and Theoretical Prediction and Analysis of Modified Sites by Molecular Dynamics Simulation

ZHAO Jun, LI Xue-Qin, XIU Zhi-Long*

Department of Bioscience and Biotechnology, Dalian University of Technology, Dalian 116024, China

Abstract:

Hirudin, a remarkably stable molecule with blood anticoagulant activity, is the most potent thrombin inhibitor in nature. But the short half life in blood plasma limits the application of hirudin in medical care. PEGylation is widely used to prolong the half life of proteins and peptides in plasma. However, the potential PEGylation sites of hirudin are numerous and it is difficult to confirm the actual PEGylation sites. In this paper, based on our experiment results of PEGylated hirudin in solution phase PEGylation and on-column PEGylation, hirudin and hirudin/thrombin complex had been simulated using molecular dynamics to predict the Lys PEGylation sites of hirudin. The results show that during the liquid-phase PEGylation, lysine residues are easy to be PEGylated except for Lys47, while during the solid-phase PEGylation, only Lys35 and Lys27 are easy to be PEGylated. And the PEGylation product can be stable when Lys35 is chosen to be the PEGylation site.

Keywords: Hirudin; Molecular dynamics simulation; PEGylation; Solvent accessible surface

收稿日期 2008-03-28 修回日期 网络版发布日期

DOI:

基金项目:

国家自然科学基金(批准号: 20176005)资助.

通讯作者: 修志龙, 男, 博士, 教授, 博士生导师, 主要从事生物催化转化与生物分离研究. E-mail: zhlxiu@dlut.edu.cn

作者简介:

参考文献:

[1]Markwardt F., Walsmann P.. Hoppe-Seyler's Z. Physiol. Chem.[J], 1958, 312: 85—98
[2]Rydel T. J., Ravichandran K. G., Tulinsky A., *et al*.. Science[J], 1990, 249: 277—280
[3]Abuchowski A., McCoy J. R., Palczuk N. C., *et al*.. J. Biol. Chem.[J], 1977, 252: 3582—3586
[4]Qin H. N., Xiu Z. L., Zhang D. J., *et al*.. Chinese J. Chem. Eng.[J], 2007, 15(4): 586—590
[5]ZHAO Xi(赵熹), HUANG Xu-Ri(黄旭日), SUN Chia-Chung(孙家锺). Chem. J. Chinese Universities(高等学校化学学报)[J], 2008, 29(4): 819—823
[6]Laemmli U. K.. Nature[J], 1970, 227: 680—685
[7]Chen H. Y., Xing Z. L., Li Y. Y.. Biotechnology[J], 2002, 12(6): 24—25
[8]Lowry O. H., Rosebrough N. J., Farr A. L., *et* al.. J. Biol. Chem.[J], 1951, 193: 265—275

[9]Vitali J., Martin P. D., Malkowski M. G., *et al*.. J. Biol. Chem.[J], 1992, 267: 17670—17678
[10]Berendsen H. J. C., van der Spoel D., van Drunen R.. Comp. Phys. Commun.[J], 1995, 91: 43—56
[11]Lindahl E., Hess B., van der Spoel D.. J. Mol. Mod.[J], 2001, 7: 306—317
[12]Li H., Robertson A. D., Jensen J. H.. Proteins[J], 2005, 61: 704—721
[13]Powers N., Jensen J. H.. J. Biomol. NMR[J], 2006, 35: 39—51
[14]Porter M. A., Hall J. R., Locke J. C, *et al*.. Proteins[J], 2006, 63: 621—635
[15]Davies M. N., Toseland C. P., Moss D. S., *et al*.. BMC Biochem.[J], 2006, 7: 18—19
[16]Berendsen H. J. C.; Eds: Meyer M., Pontikis V.. Computer Simulations in Material Science[M], Dordrecht: Kluwer Academic Publishers, 1991: 139—155
[17]Berendsen H. J. C., Postma J. P. M., DiNola A., *et al*.. J. Chem. Phys.[J], 1984, 81: 3684—3690
[18]Darden T., York D., Pedersen L.. J. Chem. Phys.[J], 1993, 98: 10089—10092
[19]Essmann U., Perera L., Berkowitz M. L., *et al*.. J. Chem. Phys.[J], 1995, 103: 8577—8593
[20]Ryckaert J. P., Ciccotti G., Berendsen H. J. C.. J. Comp. Phys.[J], 1977, 23: 327—341

本刊中的类似文章

文章评论

序号	时间	反馈人	邮箱	标题	内容

men's lacoste

women's lacos

lacoste sh