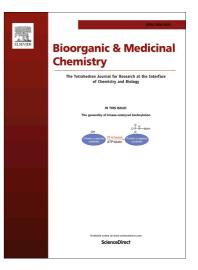
Accepted Manuscript

3-Arylpropionylhydroxamic acid derivatives as *Helicobacter pylori* urease inhibitors: Synthesis, molecular docking and biological evaluation

Wei-Kang Shi, Rui-Cheng Deng, Peng-Fei Wang, Qin-Qin Yue, Qi Liu, Kun-Ling Ding, Mei-Hui Yang, Hong-Yu Zhang, Si-Hua Gong, Min Deng, Wen-Run Liu, Qiu-Ju Feng, Zhu-Ping Xiao, Hai-Liang Zhu

PII:	S0968-0896(16)30569-7
DOI:	http://dx.doi.org/10.1016/j.bmc.2016.07.052
Reference:	BMC 13165
To appear in:	Bioorganic & Medicinal Chemistry
Received Date:	5 July 2016
Revised Date:	22 July 2016
Accepted Date:	23 July 2016



Please cite this article as: Shi, W-K., Deng, R-C., Wang, P-F., Yue, Q-Q., Liu, Q., Ding, K-L., Yang, M-H., Zhang, H-Y., Gong, S-H., Deng, M., Liu, W-R., Feng, Q-J., Xiao, Z-P., Zhu, H-L., 3-Arylpropionylhydroxamic acid derivatives as *Helicobacter pylori* urease inhibitors: Synthesis, molecular docking and biological evaluation, *Bioorganic & Medicinal Chemistry* (2016), doi: http://dx.doi.org/10.1016/j.bmc.2016.07.052

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

ACCEPTED MANUSCRIPT

3-Arylpropionylhydroxamic acid derivatives as *Helicobacter pylori* urease inhibitors: Synthesis, molecular docking and biological evaluation

Wei-Kang Shi,^a Rui-Cheng Deng,^a Peng-Fei Wang,^b Qin-Qin Yue,^a Qi Liu,^a Kun-Ling Ding,^a

Mei-Hui Yang,^a Hong-Yu Zhang,^a Si-Hua Gong,^a Min Deng,^a Wen-Run Liu,^a Qiu-Ju Feng,^a

Zhu-Ping Xiao,^{a*} Hai-Liang Zhu^{a, b}*

^aCollege of Chemistry and Chemical Engineering, Jishou University, Jishou 416000, P. R. China
^bState Key Laboratory of Pharmaceutical Biotechnology, Nanjing University, Nanjing 210093, P. R. China

Abstract: *Helicobacter pylori* urease is involved in several physiologic responses such as stomach and duodenal ulcers, adenocarcinomas and stomach lymphomas. Thus, inhibition of urease is taken for a good chance to treat *H. pylori*-caused infections, we have therefore focused our efforts on seeking novel urease inhibitors. Here, a series of arylpropionylhydroxamic acids were synthesized and evaluated for urease inhibition. Out of these compounds, 3-(2-benzyloxy-5-chlorophenyl)-3-hydroxypropionylhydroxamic acid (d24) was the most active inhibitor with IC₅₀ of 0.15±0.05 μ M, showing a mixed inhibition with both competitive and uncompetitive aspects. Non-linear fitting of kinetic data gives kinetics parameters of 0.13 and 0.12 μ g·mL⁻¹ for Ki and Ki', respectively. The plasma protein binding assays suggested that d24 exhibited moderate binding to human and rabbit plasma proteins.

Keywords: 3-Arylpropionylhydroxamic acid; *H. pylori* urease inhibitor; Plasma protein binding; Kinetics study; Non-linear fitting

^{*} Corresponding author. E-mail address: xiaozhuping2005@163.com

^{*} Corresponding author. E-mail address: zhuhl@nju.edu.cn

Download English Version:

https://daneshyari.com/en/article/7777742

Download Persian Version:

https://daneshyari.com/article/7777742

Daneshyari.com