

2-alkylthio-5-(nitroaryl)-1,3,4-thiadiazole derivatives as anti-*Helicobacter pylori* agents: investigation of structure-activity relationship

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Background and Aims: Nitro-containing heteroaromatic derivatives which are structurally related to nitroimidazole family (Metronidazole) are being extensively evaluated against *Helicobacter pylori* isolates. On the other hand, 1,3,4-thiadiazole derivatives demonstrated promising antibacterial potential. In present study, we evaluated anti-*H. pylori* activity of novel hybrid molecules bearing nitroaryl and 1,3,4-thiadiazole moieties. **Methods:** Anti-*H. pylori* activity of novel 5-(5-nitroaryl)-1,3,4-thiadiazole derivatives bearing different bulky alkylthio side chains at C-2 position of thiadiazole ring, were assessed against three different metronidazole resistant *H. pylori* isolates by paper disk diffusion method.

Results: Most of compounds demonstrated moderate to strong inhibitory response especially at 25µg/disk. The structure-activity relationship study of compounds demonstrated that introduction of different alkylthio moieties at C-2 position of thiadiazole ring; alter the inhibitory activity which is mainly dependent on the type of C-5 attached nitroheterocyclic ring. The promising compound of this scaffold, bearing 1-methyl-5-nitroimidazole moiety at C-5 and α -methylbenzylthio side chain at C-2 position of thiadiazole ring, demonstrated strong inhibitory response against metronidazole resistant *H. pylori* isolates at 12.5µg/disk (the inhibition zone diameter at all evaluated concentrations (12.5- 100 µg/disk) is >50mm).

Conclusions: Novel 5-(5-nitroaryl)-1,3,4-thiadiazole scaffold bearing different C-2 attached thio-pendant moieties with promising anti-*H. pylori* potential was identified. Among different nitroheterocycles, 5-nitrofuran and 5-nitroimidazole moieties are preferable for substitution at C-5 position of 1,3,4-thiadiazole ring. Introduction of different alkylthio side chains at C-2 position of central ring alter the inhibitory activity which is mainly dependent on the type of C-5 attached nitroheterocyclic ring.

Keywords: Thiadiazole; Anti; *Helicobacter pylori*; SAR