Synthesis and in vivo Hypoglycemic Activities of 3-Arylsulfonylimidazolidine-2,4-diones

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Diabetes is one of the major killers of our time, with people in South-east Asia and Western Pacific being the most at risk [1]. Sulfonylureas have been available for the treatment of diabetes and associated complications since the early 1950s [2]. Imidazolidine-2,4-diones on the other hand, are cyclic ureas and are known aldose reductase inhibitors [3]. N-Arylsulfonyl derivatives of imidazolidine-2,4-diones, having both a sulfonyl moiety and a urea core, may be the molecules of choice to treat diabetes and associated complications.

The synthesis of 3-arylsulfonylimidazolidine-2,4-diones (2a-p) was achieved by the reaction of imidazolidine-2,4-diones (1a-e) with arylsulfonyl chlorides in the presence of triethyl amine. Imidazolidine-2,4-diones (1a-e) were in turn synthesized from corresponding ketones. The synthesized compounds were characterized using spectroanalytical techniques. The hypoglycemic activity of compounds was evaluated using alloxanized diabetic rats model. Compound 2a was found more potent than the standard drug (glipizide). The hypoglycemic activity of compound 2b was also comparable to the standard whereas moderate activity was observed for compound 2e.

\[ R \begin{array}{c}
\text{HN} \\
\text{O} \\
\text{S} \\
\text{O} \\
\text{Ar}
\end{array} \]

\[
\begin{align*}
2a & : R = \text{CH}_3; \ Ar = 4-\text{ClC}_6\text{H}_5 \\
2b & : R = \text{C}_6\text{H}_5; \ Ar = 4-\text{ClC}_6\text{H}_5 \\
2c & : R = \text{C}_6\text{H}_5; \ Ar = 4-\text{BrC}_6\text{H}_5 \\
2d & : R = \text{C}_6\text{H}_5; \ Ar = 4-\text{CH}_3\text{C}_6\text{H}_5 \\
2e & : R = \text{C}_6\text{H}_5; \ Ar = 4-\text{CH}_3\text{OC}_6\text{H}_5 \\
2f & : R = \text{C}_6\text{H}_5; \ Ar = 2-\text{naphthyl} \\
2g & : R = 4-\text{FC}_6\text{H}_5; \ Ar = 4-\text{CH}_3\text{C}_6\text{H}_5 \\
2h & : R = 4-\text{FC}_6\text{H}_5; \ Ar = 4-\text{BrC}_6\text{H}_5 \\
2i & : R = 4-\text{FC}_6\text{H}_5; \ Ar = 4-\text{CH}_3\text{OC}_6\text{H}_5 \\
2j & : R = 4-\text{FC}_6\text{H}_5; \ Ar = 4-\text{ClC}_6\text{H}_5 \\
2k & : R = 4-\text{BrC}_6\text{H}_5; \ Ar = 4-\text{CH}_3\text{C}_6\text{H}_5 \\
2l & : R = 4-\text{BrC}_6\text{H}_5; \ Ar = 4-\text{CH}_3\text{OC}_6\text{H}_5 \\
2m & : R = 4-\text{BrC}_6\text{H}_5; \ Ar = 4-\text{ClC}_6\text{H}_5 \\
2n & : R = 4-\text{BrC}_6\text{H}_5; \ Ar = 4-\text{ClC}_6\text{H}_5 \\
2o & : R = 4-\text{ClC}_6\text{H}_5; \ Ar = 4-\text{CH}_3\text{OC}_6\text{H}_5 \\
2p & : R = 4-\text{ClC}_6\text{H}_5; \ Ar = 4-\text{BrC}_6\text{H}_5
\end{align*}

REFERENCES