

Review Form 1.6

Journal Name:	Journal of Pharmaceutical Research International
Manuscript Number:	Ms_JPRI_77713
Title of the Manuscript:	An efficient synthesis of 4-aminomethyl-1-(2-phenylethyl)-piperidin-4-ol: A key intermediate in Fenspiride HCl synthesis
Type of the Article	Original Research Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound. To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	<p>The work is impressive and the results are interesting. However, some points deserve to be clarified before publication. I recommend the publication with major revisions as follows:</p> <p>The article confers scalable manufacturing process... The article confers a scalable manufacturing process.</p> <p>is a main building block in Fenspiride HCl synthesis.... is the main building block in Fenspiride HCl synthesis.</p> <p>produces hazardous waste and also needs to be handled with at most care.... produce hazardous waste, and also need to be handled with most care.</p> <p>environment friendly.. environment-friendly.</p> <p>It also eliminates toxic, sensitive and hazardous reagents and make the process.... It also eliminates toxic, sensitive, and hazardous reagents and makes the process.</p> <p>It has antitussives properties and mainly used.... It has antitussives properties and is mainly used. It is also been used for treatment of allergy within otolaryngological... It is also been used for the treatment of allergy within otolaryngology.</p> <p>The detailed literature survey for Fenspiride HCl (1)... In the detailed literature survey for Fenspiride HCl (1).</p> <p>for the synthesis Fenspiride HCl (1)... for the synthesis of Fenspiride HCl (1).</p> <p>use of several hazardous reagents and difficult to handle... use of several hazardous reagents and is difficult to handle.</p> <p>detailed review of literature revealed... a detailed review of the literature revealed.</p> <p>beta hydroxy... beta-hydroxy.</p> <p>Finally BOC anhydride is used... Finally, BOC anhydride is used.</p> <p>Nitroalkanes [12] are have peculiar properties.... Nitroalkanes [12] have peculiar properties. which are very shock sensitive and may undergo for explosion on dry condition.... which is very shock-sensitive and may undergo the explosion in dry condition.</p> <p>under hydrogenation condition using hydrazine... under hydrogenation conditions using hydrazine.</p> <p>purity (>99.7%) complying to ICH guidelines.... purity (>99.7%) complying with ICH guidelines.</p> <p>Bio systems... Biosystems.</p> <p>The resulting mixture was stirred at 25 °C to 35 °C till completion of.... The resulting mixture was stirred at 25 °C to 35 °C till the completion of.</p> <p>followed by addition of toluene.... followed by the addition of toluene.</p> <p>till completion of reaction, as monitored by HPLC.... till completion of the reaction, as monitored by HPLC.</p> <p>followed by addition of water and filtration.... followed by the addition of water and filtration.</p> <p>Gradual addition of ethyl acetate to the residue separated out fenspiride base... The gradual addition of ethyl acetate to the residue separated out the fenspiride base.</p> <p>acetate and dried under vacuum.... acetate and dried under a vacuum.</p> <p>The available literature of Fenspiride hydrochloride gives a numerous methods of preparation which are full of hazardous reagent.... The available literature on Fenspiride hydrochloride gives numerous methods of preparation that are full of hazardous reagents.</p> <p>As part of our ongoing efforts toward developing efficient... As part of our ongoing efforts toward developing an efficient.</p> <p>simpler reagents/reaction conditions that results in... simpler reagents/reaction conditions that result in.</p> <p>To make the hazard free the manufacturing of Fenspiride HCl... To make the hazard-free</p>	

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	<p>manufacturing of Fenspiride HCl.</p> <p>Retrosynthetic presentation of proposed route.... Retrosynthetic presentation of the proposed route.</p> <p>The BOC-protection was attempt the cyclisation... The BOC-protection was attempted the cyclisation.</p> <p>intermediate (14) under basic condition.... intermediate (14) under basic conditions.</p> <p>The advance process avoids... The advanced process avoids.</p> <p>and the lethal reagents like palladium... and lethal reagents like palladium.</p> <p>simplicity in industrial scale.... simplicity on an industrial scale.</p> <p>very easy to handle on large scale application.... very easy to handle on large-scale applications.</p>	
Minor REVISION comments		
Optional/General comments		

PART 2:

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Are there ethical issues in this manuscript?	<i>(If yes, Kindly please write down the ethical issues here in details)</i>	

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