

Studies on Pseudoephedrine Hydrochloride as a Sympathomimetic Alternative to Phenylpropanolamine in Decongestant Formulations.

J.N. Idih, M.Sc.¹; I.O. Adeleke, M.Sc.²; and C.I. Igwilo, Ph.D.¹

¹School of Pharmacy, College of Medicine, University of Lagos, Lagos, Nigeria.

²Faculty of Pharmaceutical Sciences, University of Jos, Nigeria.

E-mail: ioadeleke@yahoo.com*

ABSTRACT

In this study, an attempt has been made to replace phenylpropanolamine with pseudoephedrine hydrochloride as active ingredient in tablets. The in-house SKG Pharma assay tests on tablets containing pseudoephedrine hydrochloride and phenylpropanolamine tablets (marketed in Nigeria) gave results of 98.32% and 95.93%, respectively. For the assay of pseudoephedrine, the standard for the percentage of the stated amount in the tablet is $100\% \pm 10\%$ while the result obtained from this study is 95.93%. This shows that it conforms to the standard and as a result, passes the assay test. For the assay of phenylpropanolamine, the standard is $100\% \pm 10\%$. The result obtained is 98.32%. From these results, it can be deduced that pseudoephedrine; a stereoisomer of ephedrine with similar but less potent pharmacological activity, is a safer molecule in tablet preparation than phenylpropanolamine.

(Keywords: phenylpropanolamine, PPA, pseudoephedrine hydrochloride, active ingredient, tablets, assay/physical tests, pharmacology, activity)

INTRODUCTION

For several decades, the ingredient phenylpropanolamine (PPA) included in pharmaceutical formulations has been fraught with controversy. Many who used PPA escaped without adverse effects; however, its side-effect profile was too high for general consumer safety. These serious adverse reactions reported in the medical literature were equally disturbing to concerned medical professionals (PPA Drug Information, 2011). Nevertheless, non-prescription product manufacturers continued to assert that the substance was safe and effective

for both nasal congestion and weight loss. Many of the best selling products contained the ingredient, and it was widely marketed to the lay public, despite preliminary data suggesting that it was responsible for serious patient harm.

Its main clinical use is as a nasal decongestant when it may be used alone or in combination with other agents for the symptomatic relief of cold symptoms and it is usually administered orally for such purposes. Adverse effects of PPA are essentially those of adrenergic stimulation, but hypertensive reactions and stimulation of the central nervous system have occurred (CanTox Report, 2011). And it is due to this effect that the United States Food and Drug Administration (FDA) eventually asked manufacturers to withdraw products containing phenylpropanolamine. It also requested that all drug companies discontinue marketing products containing phenylpropanolamine, because it caused serious bleeding in the brain known as a haemorrhagic stroke. Women were found to be more likely to experience this problem, though men were also at risk. Phenylpropanolamine is a sympathomimetic drug and is an agent that has actions similar to those that follow stimulation of post ganglionic sympathetic or adrenergic nerves (CanTox Report, 2011).

The prerequisite for sympathomimetic that can strictly be used as a nasal decongestant is the presence of a catechol nucleus and amino-containing side chain. A catechol nucleus has a benzene ring with two adjacent hydroxyl groups. The possible organic compounds with a catechol nucleus (as the precursor) that can substitute for phenylpropanolamine include xylometazoline hydrochloride, tymazoline hydrochloride, tetrahydrozoline hydrochloride, tuaminoheptane sulphate, tramazoline hydrochloride, cyclopetamine hydrochloride, nahazoline hydro-

chloride, phenylpropylmethlamine, propylhexedrine, and pseudoephedrine hydrochloride.

All these compounds, with the exception of cyclopetamine hydrochloride and pseudoephedrine hydrochloride are used as nasal decongestants only due to some elementary pharmacological and pharmaceutical reasons. But the only other non-nasal use of cyclopetamine hydrochloride is in the injectable form and for a totally different purpose. Pseudoephedrine hydrochloride is a stereoisomer of ephedrine and is a safer molecule than PPA. It is an almost colorless white crystalline powder with a bitter taste and faint characteristic odor. It is a naturally occurring alkaloid from the ephedra species. Pseudoephedrine hydrochloride is used therapeutically as a decongestant and bronchodialator.

The aim of this work is to define the ingredient phenylpropanolamine (PPA) as used in most pharmaceutical products and to study another sympathomimetic, pseudoephedrine hydrochloride as a possible safer alternative in pharmaceutical preparations (Dickerson *et al.*, 1978; Young *et al.*, 1980).

MATERIALS

This study utilized pseudoephedrine hydrochloride tablets, phenylpropanolamine containing tablets, lactose, methyl paraben, maize starch I, povidon K30, magnesium stearate, maize starch II, and de-ionized water.

METHODS

Preparation of Tablets

The tablets were prepared by wet granulation method. 60 mg pseudoephedrine hydrochloride, 11.36 mg lactose, 0.4 mg methyl paraben, 4mg povidon K30 (per tablet) were screened and emptied into a ribbon mixer and blended for 20 mins. at first and later for 5 mins. Using 30 mg of maize starch I per tablet, the mucilage was prepared, and added to the blended ingredients in a V-shaped mixer. This was blended for 30 mins to form a wet mass which was screened and dried in a fluidized bed drier at temperature of 50°C to a moisture content of 1-2%.

The dried granules were screened, after which 2mg magnesium stearate and 10mg maize starch II were added per tablet and blended for 5 mins. The granules were then compressed to obtain a tablet weight of 220 ± 11 mg, friability less than 1%, disintegration time less than 10 mins and hardness of 4 to 8 Kp. The physical properties of the tablets were then carried out.

Pseudoephedrine Assay

20 tablets were weighed and powdered. 1.8333 g of the sample was weighed which is equivalent to 0.5 g of pseudo-ephedrine hydrochloride. This was transferred into 250 ml conical flask; 50 ml of distilled water was added to the powdered sample and it was then vigorously shaken for 20 mins. The mixture was now filtered. The filtrate was titrated with 0.1 M sodium hydroxide using phenolphthalein as indicator.

Phenylpropanolamine Assay

40 tablets having a composition of 500 mg paracetamol, 25 mg phenylpropanolamine and 2 mg of chlorpheniramine maleate per tablet were weighed and powdered. 12 g of the powdered sample which is equivalent to 0.5 g of phenylpropanolamine was transferred into a 250 ml conical flask. 50ml of distilled water was added to the powdered sample, vigorously shaken for 20 mins. and filtered. The filtrate was titrated with 0.1 M sodium hydroxide using phenolphthalein as indicator.

RESULTS

The results obtained from the assay as well as the physical properties of the tablets are shown in Table 1.

DISCUSSION

The average weight of batch of pseudoephedrine tablet was determined as 229.8 mg with weight variations of -1.22 to +0.96. The weight variation determined is within the permitted limit and this indicates that the batch of tablets met pharmacopoeial requirements for weight variation. The hardness and friability values determined were 5.9 Kp and 0.33% for pseudoephedrine tablet and that for

phenylpropranolamine tablet were 4.9 Kp and 0.61%.

Table 1: Assay/Physical Properties of Tablets.

S/N	Parameters	Pseudo-ephedrine Tablet	Phenyl-propranolamine Tablet
1.	Average Weight (mg)	229.8	610
2.	Weight Variation (%)	-1.22 to +0.96	-0.49 to +0.33
3.	Hardness (Kp)	5.9	4.9
4.	Disintegration time (mins)	3 mins 50 secs	3 mins
5.	Friability (%)	0.33	0.61
6.	Thickness (mm)	3.73	6.53
7.	Diameter (mm)	8.60	12.60
8.	Assay concentration (%)	95.93	98.32

These results show that the friability of the pseudoephedrine tablet is higher than that of phenylpropranolamine tablet. This is expected due to the fact that the harder the tablet the lower the tendency for it to chip, cap or break. The diameters of the batches of tablets differ and this may be due to difference in diameters of the tableting machine die cavity used. The disintegration time determined for both tablets fall below the upper limit of 15 mins. standard required (Aulton, 1999).

For the assay of pseudoephedrine, the standard for the percentage of stated amount in the tablet is $100\% \pm 10\%$ while the result obtained from this study is 95.93%. This shows that pseudoephedrine tablets conform to the standard and as a result, passes the assay test. For the assay of phenylpropranolamine, the standard is $100\% \pm 10\%$. The result obtained is 98.32%. This is a good assay result and therefore passed the assay test. This result complies with the standard.

CONCLUSIONS

The study has shown that pseudoephedrine has physical properties similar to phenylpropranolamine. And since the results obtained met pharmacopoeial specification, pseudoephedrine could safely serve as a substitute for phenylpropranolamine. Pseudoephedrine has a similar but less potent pharmacological activity

and so could serve as a safer molecule than phenylpropranolamine.

REFERENCES

1. Aulton, M.E. 1999. *Pharmaceutics: The Science of Dosage form Design. 9th Edition.* Churchill Livingstone: London, UK
2. CanTox Report. 2011. <http://www.crnusa.org/pdfs/cantoxreport.9/28/11>.
3. Dickerson, J., D. Perrier, M. Mayersolin, and R. Bressler.1978. "Dose Tolerance and Pharmacokinetic Studies of L – (+) Pseudoephedrine Capsules in Man". *European Journal of Clinical Pharmacology.* 14:253-259.
4. PPA Drug Information. 2011. <http://www.drugs.com/mmx/phenylpropranolamine-hydrochloride.html>. 9/28/11.
5. Young, D.W. and G.A. Lethy.1980. "Dose Response Study of the Nasal Decongestant with Electron Captures Detection". *Journal of Chromatography.* 222: Biomedical Application. 11:297-302.

ABOUT THE AUTHORS

Mr. J.N. Idih, holds a M.Pharm. degree in Pharmaceutics. He has over 15 years experience in pharmaceutical practice.

Mrs. I.O. Adeleke, holds a M.Pharm. degree in Pharmaceutics. She has over 15 years experience in pharmaceutical practice.

Professor (Mrs.) C.I. Igwilo, holds a Ph.D. in Pharmaceutics. She has over 25 years teaching and research work experience in Pharmaceutics.

SUGGESTED CITATION

Idih, J.N., I.O. Adeleke, and C.I. Igwilo. 2012. "Studies on Pseudoephedrine Hydrochloride as a Sympathomimetic Alternative to Phenylpropranolamine in Decongestant Formulations". *Pacific Journal of Science and Technology.* 13(1):473-475.

 [Pacific Journal of Science and Technology](http://www.akamaiuniversity.us/PJST.htm)