Determination of pyrolysis products of efavirenz by Gas Chromatography Mass Spectrometry

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Introduction

Efavirenz is an anti-retro viral drug with notable psychedelic effects. It is being used as the main ingredient of Whoonga (a new recreational drug) which is slowly becoming common in the townships of South Africa and its neighbouring countries. Whoonga is distributed as a fine powder which is mixed with cannabis (leaf or resin material) and /or tobacco for smoking in order to increase or prolong the narcotic effects [4]

Fig 3. Whoonga mixture [4]

The ability to analyse the thermal decomposition products of the compound are of interest as a potential mechanism for confirming the use of the drug. However such analysis is challenging and previous literature details a number of analytical methods for the quantification of the compound using, primarily, soft ionisation techniques [1], [2], [3] (i.e. High Performance Liquid Chromatography) which do not lend themselves easily to analysis of heated products.

Gas Chromatography is the preferred technique for the analysis of thermally degraded (pyrolysis) products associated with the illicit smoking of the drug, however, there are very few gas chromatographic methods reported in the literature. This study addresses this deficiency and reports a new gas chromatographic analytical method.

Methodology

A new chromatographic method for the analysis of efavirenz was devised through the modification of existing literature based methods. The analysis was preformed using an Agilent 5975/5977 Series Gas Chromatography /Mass Spectrometry.

The following method was used:

Component	Inlet	Oven	Column	Transfer line	MS Quadruple
Temperature profile	280	260	280	250	150

Injection mode	Gas flow rate	Injection volume	Column Type	Library
Split (10:1)	20µL/min	2µL	DB -1 ms	NIST 2008

The initial oven temperature was set at 100^{o}c and was ramped once (rate 10^{o}c/min) to 260^{o}C resulting in a total run time of 27minutes.

Instrument selectivity and repeatability of analysis was performed by injecting 2 µL of a Hydrocarbon Grob (0.5 µg/mL) test mixture six times. The %RSD values were then calculated for each peak in the standard to assess repeatability of the method.

Analysis of a standard solution of of efavirenz (1mg/mL) in methanol was then undertaken on the validated system.

Further method specificity and selectivity were tested by injecting a 1mg/mL laboratory standard mixture of efavirenz and two cannabinoids (cannabidiol and cannabinol) into the instrument.

References

1. Villan P, Feroggio M, Gianelli L, et al. Ther Drug Monit. 2001;23:380-388.
2. Langmann P, Schirmer D, Vath T, et al. J Chromatogr B Analyt Technol Biomed Life Sci. 2002;767:69-74.
3. Veldkamp et al JChrom B Bioned Sci Apple 1999, 734, 55-61
4. ZAMAKHOSI THINA SHEMBE, The effects of whoonga on the learning of affected youth in kwa-dabeka township, Master of science dissertation, University of South Africa, 2013
5. Rentsch KM. J Chromatogr B Analyt Technol Biomed Life Sci. 2003;788:339-350.

Results and Discussions

Components of the Grob mixture were fully resolved (fig.4 below) which indicates that the method is both selective and specific. Mean %RSD values for each compound across the six repeat injections ranged from 2.47% - 4.67%. This indicates that there is no significant variation between replicate results.

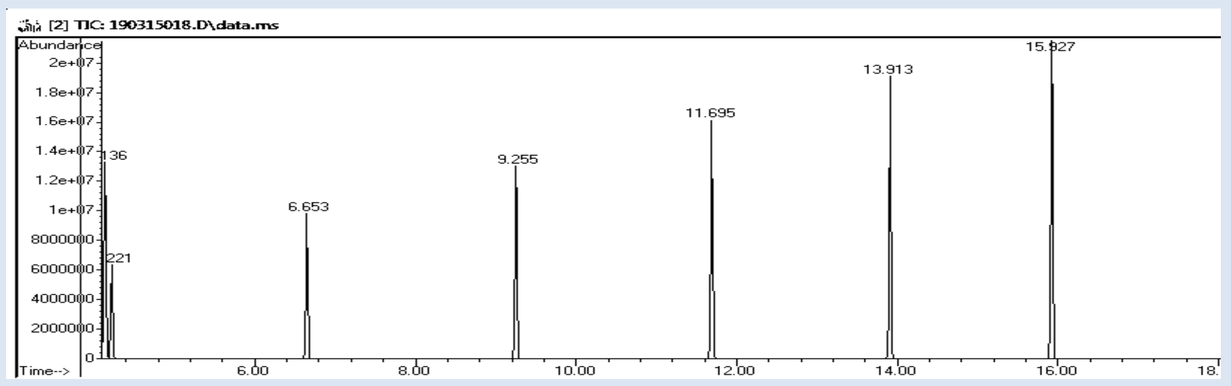


Fig 2. Components of the Grob test mixture

Efavirenz was detected at 16.967 minutes with main ions identified at *m/z 315, 246, 243, 224, 180 and 167 (fig 3 below)*

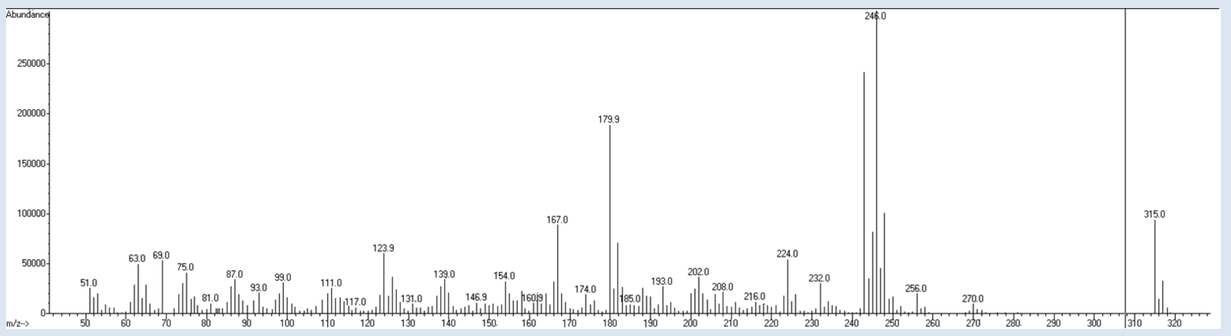
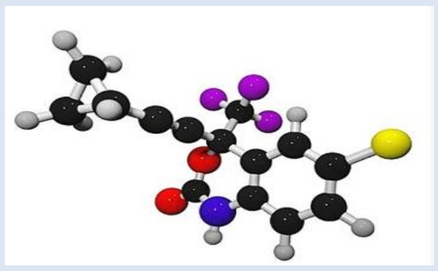


Fig 3. *m/z* ions of efavirenz



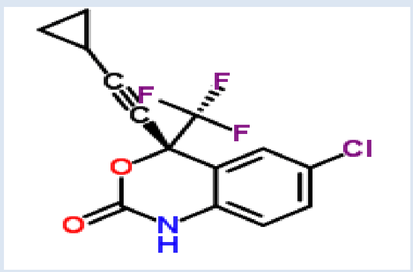


Fig 4a and 4b. 3D conformer and 2D chemical structure of efavirenz [1]

The method was also able to distinguish between the three compounds in the standard mixture made in the laboratory (fig. 5 below) which again supports its specificity and selectivity.

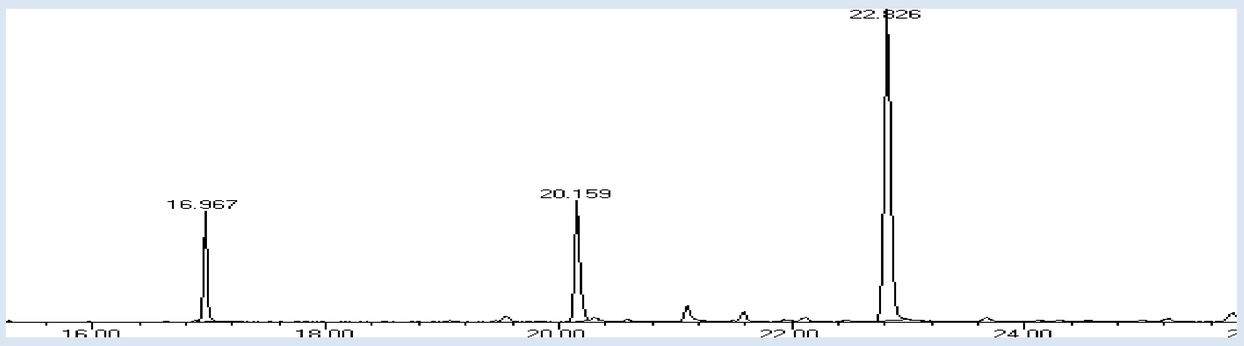


Fig 5. Chromatogram showing efaviranz at 16.9 minutess and the two cannabinoids (CBN,CBD) at 20.1 and 22.8 minutes

Conclusions

A method for the detection and identification of pyrolysis products of efavirenz from pharmaceutical (tablet) formulations was developed using Gas Chromatography Mass Spectrometry technique. This method will now be used for the further analysis of efavirenz and the elucidation of its thermal decomposition products. It can also be used the detection of cannabis combinations in street drugs.