



The Characterization of 'Legal Highs' Available from Head Shops in Dublin



P.V. Kavanagh¹, S. McNamara², D. Angelov¹, S. McDermott¹, D. Mullan¹ and S.A. Ryder³

¹ Department of Pharmacology and Therapeutics, School of Medicine, Trinity Centre for Health Sciences, St. James's Hospital, Dublin 8.

² Drug Treatment Centre Board, Pearse Street, Dublin 2.

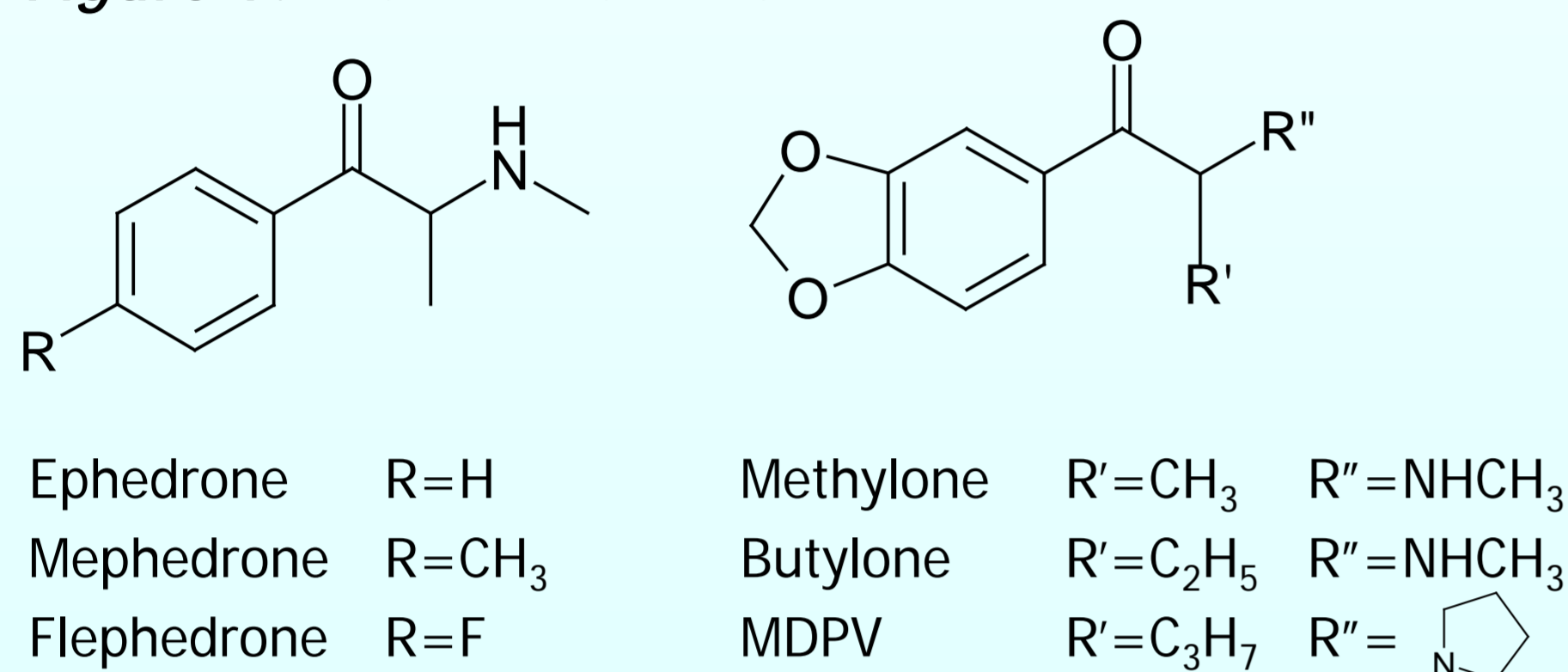
³ School of Pharmacy and Pharmaceutical Sciences, Trinity College, Dublin 2.

Introduction

The past two years have seen an explosion in the number of head shops in Ireland, including Dublin.^{1,2} Since benzylpiperazine (BZP) was outlawed in March 2009 there has been a significant increase in the number of drugs with similar stimulant effects being legally sold as 'bath salts' or 'plant food' in head shops around Dublin in an attempt to fill the vacuum created by the BZP ban. New brands regularly appear and anecdotal reports suggest that the constituents of a given product may vary.

These 'legal highs' are mainly cathinone derivatives (methyldone, methylenedioxypropylvalerone (MDPV), butylone, flephedrone and mephedrone) which possess a similar chemical structure to amphetamines, and are usually sold either as capsules or in loose powder.³

Figure 1: Cathinone derivatives



The drugs are most commonly administered orally or by insufflation and users report increased alertness, euphoria, excitement and a feeling of stimulation, an urge to talk, openness, and empathy. Negative effects such as dehydration and erectile dysfunction are common, and serious adverse reactions such as severe discolouration of the knees attributable to vascular damage ('blue knees'), cardiac arrhythmias, and paranoia have also been reported⁴⁻⁶. Recently, mephedrone use has also been linked to suicide.⁷

The purpose of this study was to identify the constituents in products on the Dublin market. As mephedrone is considered to be one of the more dangerous cathinones, having recently been associated with several deaths⁸⁻¹², we also determined the concentration of mephedrone in samples where this was found to be an active constituent.

Experimental

Samples and reference materials

Eighteen samples were obtained from head shops in Dublin, selected based on reported popularity and employees' recommendations of the "best buzz" available. These were Blow, The Business, Charge+, Craic, Diablo XXX, The Dog's Bollox, Doves, Doves Ultra, Hurricane Charlie, Ivory Wave, Magic, Mint Mania, Oceanic Deeper, Sextacy, Snow, Summer Daze, White Ice and Wild Cat.

For the identification of methyldone, MDPV and flephedrone, a reference library with retention time and mass spectral data was compiled from the analysis of characterized specimens of 'bath salts'/'plant food' provided by the Drug Treatment Centre Board laboratory. Also included in the library were butylone, caffeine, lignocaine and benzocaine which were obtained as pure reference standards, and mephedrone which was purified and characterized in our own laboratory.

All chemicals and solvents used were of analytical reagent grade obtained from Sigma Aldrich Ltd. (Dublin).

GC/MS conditions

GC-MS analyses were performed using an Agilent 6890 gas chromatograph with split-splitless injection (2 µl injected) and a HP-5MS column (30 m x 0.25 mm, 0.25 µm film thickness). Helium was used as the carrier gas at a flow rate of 1.0 ml/min. The GC was coupled to an Agilent 5973 MSD (EI, 70eV, TIC mode scanning m/z 40-800). The following temperature programme was used: 90°C for 1 min, 15°C/min to 280°C, 280°C for 6 min, 10°C/min to 300°C, 300°C for 13.33 min, injector port 280°C, transfer line 280°C.

Sample Preparation

An accurately weighed sample (1 mg) was placed in a 2 ml centrifuge tube and sonicated with methanol (1 ml) for 5 min. The mixture was then centrifuged for 5 min at 10,000 rpm, after which the supernatant was placed in a glass vial for GC/MS. All samples were analysed in duplicate.

Preparation of mephedrone hydrochloride standard

A sample of product known to contain mephedrone was extracted from basic solution into ethyl acetate. The solvent was removed and the residue was purified by flash chromatography (ethyl acetate). Evaporation of the combined fractions containing mephedrone followed by addition of methanolic HCl, re-evaporation, trituration with acetone and drying *in vacuo* afforded a white powder, fully characterized by mass spectrometry and NMR.

Quantification of mephedrone

Four samples which had been found to contain mephedrone (Diablo XXX, Blow, The Business and Wild Cat), were subjected to quantitative analysis. Water (5 ml) was added to an accurately weighed amount of each sample (1 mg). Ammonia (50 µl) and toluene (5 ml) were then added and the mixture was rotated for 10 min. After centrifugation 1 ml of the upper layer was transferred to a vial for GC/MS analysis. Concentrations were determined from a standard curve prepared in the same manner.

Results and Discussion

All the samples (n = 18) were found to contain cathinone derivatives: mephedrone (28% of products), flephedrone (17%), methyldone (22%), butylone (17%) and MDPV (22%), either in isolation or in combination. A substantial minority (39%) of the products tested also contained local anaesthetics, which may ease the pain anecdotally associated with repeated cathinone insufflation and mimic the sensation associated with cocaine use. The results of the qualitative and quantitative analysis are displayed in Tables 1 and 2.

Table 1: Active constituents detected in product samples

Product	Cathinones	Other constituents
The Business	Mephedrone	
Diablo XXX	Mephedrone	
Magic	Mephedrone	
Blow	Mephedrone	Benzocaine
Wild Cat	Mephedrone	Benzocaine, caffeine
Oceanic Deeper	Flephedrone	Lignocaine, caffeine
Charge +	Flephedrone	Lignocaine, caffeine
White Ice	Flephedrone	Lignocaine, caffeine
Snow	Methyldone	
Mint Mania	Methyldone	
Craic	Methyldone	
Dog's Bollox	Methyldone, MDPV	
Hurricane Charlie	MDPV	
Ivory Wave	MDPV	Lignocaine
Sextacy	MDPV	Lignocaine
Doves	Butylone	
Doves Ultra	Butylone	
Summer Daze	Butylone	

Table 2: Mephedrone concentration in product samples

Product	% as HCl salt	% as free base
The Business	82.2	68.1
Wild Cat	66.1	54.8
Blow	39.9	33.1
Diablo XXX	14.6	12.1

'High' doses for mephedrone taken orally or by insufflation are considered to be 250 mg and 125 mg, and this typically refers to the hydrochloride salt^{13,14}. Using one pack (500 mg of product) of The Business or Wild Cat in a single dose would result in mephedrone hydrochloride doses of 411 mg and 331 mg respectively. These are well into the 'high' dose range and the potential for significant toxicity thus arises, especially in first time users.

As such information is of use to law enforcement officers, addiction counsellors and emergency medical personnel, we have compiled it into an easy to read pictorial format as shown in Figure 2. Our work has significant clinical value, since clinicians now have a quick reference guide to the active constituent(s) in many popular brands. This will facilitate targeted treatment based on knowledge of what has been consumed, a clear advantage in light of increasing hospitalizations requiring urgent treatment such as the case of the 17-year old girl from Bray, Co. Wicklow, who presented to Loughlinstown Hospital A&E in a convulsant state in March 2010 after taking mephedrone.¹⁵

Figure 2: Drug identification poster



As mentioned earlier, discolouration of the knees ('blue knees') has been reported with mephedrone use, particularly with high dosage.⁴⁻⁶

Figure 3: Appearance of knees following mephedrone use



Erythrocyte aggregation, venous congestion, and reduction of the capillary network have previously been observed with ephedrone.¹⁶ Using our guide to help identify cases where cathinones have been administered, the nature and extent of the association between vascular problems and cathinone use is likely to become clearer.

Conclusion

We have successfully characterized some of the most popular legal highs available in Dublin head shops. These products were found to contain the cathinone derivatives mephedrone, methyldone, flephedrone, butylone and MDPV. The stimulant caffeine, and local anaesthetics benzocaine and lignocaine, were found in a number of samples. Mephedrone was present in just over one quarter of the samples analysed. This is of concern as media reports have linked this cathinone to several deaths.⁷⁻¹²

Our work provides a foundation for further research into these drugs' mechanisms of action, metabolism and toxicities. Such future work will be key to the management of hospitalizations associated with these drugs' misuse.

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