Kent Academic Repository

Full text document (pdf)

Citation for published version

Ferris, T.J. and Went, Michael J. (2012) Synthesis, Characterisation and Detection of Gamma-Hydroxybut
Salts. Forensic Science International, 216 . pp. 158-162. ISSN 0379-0738.

DOI

https://doi.org/10.1016/j.forsciint.2011.09.014

Link to record in KAR

http://kar.kent.ac.uk/29249/

Document Version

Author's Accepted Manuscript

Copyright & reuse
Content in the Kent Academic Repository is made available for research purposes. Unless otherwise stated all content is protected by copyright and in the absence of an open licence (eg Creative Commons), permissions for further reuse of content should be sought from the publisher, author or other copyright holder.

Versions of research
The version in the Kent Academic Repository may differ from the final published version.
Users are advised to check **http://kar.kent.ac.uk** for the status of the paper. **Users should always cite the published version of record.**

Enquiries
For any further enquiries regarding the licence status of this document, please contact:
researchsupport@kent.ac.uk

If you believe this document infringes copyright then please contact the KAR admin team with the take-down information provided at **http://kar.kent.ac.uk/contact.html**

KAR Kent Academic Repository

University of Kent

Synthesis, Characterisation and Detection of Gamma-Hydroxybutyrate Salts

Trevor J. Ferris and Michael J. Went

School of Physical Sciences, University of Kent, Canterbury, Kent, CT2 7NH, UK

Corresponding author. Tel +44 1227 823540; fax +44 1227 827558

E-mail address: m.j.went@kent.ac.uk

Abstract

Sodium, potassium, magnesium and calcium salts of gamma-hydroxybutyrate have been synthesised from gamma-butyrolactone and the corresponding group 1 or 2 hydroxide. Although the group 2 salts are non-hygroscopic, FT-IR spectroscopy and elemental analysis revealed them to be hydrated. X-ray powder diffraction was found to be a quick, non-destructive method of discriminating between the four salts. The Smith and the chlorophenol red/modified Schweppes reagent presumptive colour tests gave positive results regardless of the salt tested. Microcrystalline tests for NaGHB were in accordance with previous literature reports, but results for the other three salts were not reliable.

Keywords: GHB; crystal tests; presumptive colour tests; X-ray powder diffraction.

1. Introduction

Gamma-hydroxybutyrate (GHB) has a long history as a sleep aid, nutritional supplement, and recreational drug, and has been widely reported in the media regarding its use in the malicious act of drug facilitated sexual assault [1]. In the UK GHB was classified as a Class C controlled substance as of June 2003 under the Home Office Misuse of Drugs Act (1971) which makes it an offence to unlawfully supply, intend to supply, import or export and possess GHB [2]. Gamma-butyrolactone (GBL) and 1,4-butanediol (1,4-BD) are precursors of GHB and are chemically very similar. GBL and 1,4-BD were brought under the control of the 1971 Act in 2009 [3].

GHB is commonly encountered forensically as gamma-hydroxybutyric acid or in salt form as gamma-hydroxybutyrate typically as a sodium salt [4, 5] also known as sodium oxybate. The use of "GHB" to refer to both illicit GHB and sodium oxybate has blurred the distinction in the scientific literature and the popular press [6]. Other salts including lithium, potassium, magnesium and calcium are known [7, 8, 9]. The sodium salt of GHB is the most extensively studied. It is conveniently prepared by the reaction of gamma-butyrolactone (GBL) and sodium hydroxide or it can be purchased commercially from chemical suppliers or obtained from a pharmacy with a prescription as Xyrem®. It has been characterised by a variety of instrumental techniques including IR and NMR spectroscopy [10, 11, 12, 13, 14] , as well as presumptive spot tests [15, 16] and microcrystalline tests [17, 18, 19]. The aims of this research were to explore the synthesis, characterisation and detection of the potassium, magnesium and calcium salts of GHB.

2. Materials and methods

2.1. Reagents

All reagents were prepared in reverse osmosis water. All chemicals were purchased from the following suppliers and used as received. Gamma-butyrolactone (99+ %), Acros Organics. Sodium hydroxide pellets (98.25%), VWR International. Potassium hydroxide pellets (97%) and zirconium nitrate, BDH Laboratory Supplies. Magnesium hydroxide (95%), calcium hydroxide (95%), barium nitrate (99%), calcium nitrate tetrahydrate (99%), cobalt (II) nitrate, copper (II) nitrate hemipentahydrate (98%) and iron (III) nitrate nonahydrate (> 98%), Sigma-Aldrich. Bromocresol green and red, manganous nitrate and zinc nitrate, Fisons. Acetone, methanol and ethanol (Laboratory Reagent Grades), Fisher Scientific. Methyl orange, Griffin and George. Lanthanum nitrate hydrate (99.9%), nickel (II) nitrate hexahydrate, thallium (III) nitrate trihydrate and yttrium pentahydrate (99.9%), Aldrich. Silver nitrate, Riedel-de Haen. Sodium nitrate (99%), Lancaster Synthesis.

2.2. FT-IR spectroscopy

FT-IR spectra were recorded with a Thermo Nicolet Avatar 380 FT-IR spectrometer equipped with a smart orbit ATR accessory and OMNIC 7.3 software (Thermo Electron Corp.).

2.3. X-ray powder diffraction

X-ray powder diffraction data were collected using a Bruker D8 Advance diffractometer with Cu-Kα radiation. Acquisition conditions were 40 kV and 40 mA. Scans were obtained from 5º to 70º, with step size of 0.02º and a count time of 1 s. Observed peak positions were matched against the ICDD JCPDS database.

2.4 Elemental Analysis

Elemental analysis was performed by Dr D. O. Smith at the Analysis Centre, University of Kent, using a Carlo Verba 1106 elemental analyser.

2.5. Synthesis

2.5.1. Sodium Gamma Hydroxybutyrate

NaOH (10 g, 0.25 moles) was dissolved in ethanol (166 mL) and once cooled GBL (20 mL, 0.26 moles) was added in 5 mL fractions. A white precipitate of NaGHB immediately formed and the solution was allowed to stand for 2 h before the precipitate was collected by filtration through a Büchner funnel. The precipitate was then transferred to a glass dish and dried for 5 h in an electric oven at 40 ^{o}C. The dried NaGHB powder (31.2 g, 99%) was immediately transferred to a glass air tight screw top storage container. Found: C, 38.4; H 5.3. Calc for $C_4H_7NaO_3$: C, 38.1; H, 5.6.

2.5.2. Potassium Gamma Hydroxybutyrate

KOH (14 g, 0.25 moles) was dissolved in ethanol (166 mL) and once cooled GBL (20 mL, 0.26 moles) was added in 5 mL portions. The solution was left for 2 h before addition of diethylether (120 mL). The resulting white precipitate was collected by filtration through a Büchner funnel and dried in an oven over night at 40°C. The dried KGHB (26.7 g, 76%). was removed from the oven and placed in an airtight container. Found: C, 33.9; H, 5.0. Calc for $C_4H_7KO_3$: C, 33.8; H, 5.0.

2.5.3. Calcium Gamma Hydroxybutyrate

$Ca(OH)_2$ (9.25 g, 0.125 moles) was suspended in water (25 mL) and then GBL (20mL, 0.26moles) was added slowly in 5 mL portions which caused an exothermic reaction heating the solution rapidly. The solution was then heated to 105 ºC for 15 min to remove any remaining water. The viscous residue was then mixed with acetone several times over a 24 h period. The product was then dried for 2 h at 60 ºC to afford

$Ca(GHB)_2.2H_2O$ (31.5 g, 89%). Found: C, 34.2; H, 6.8. Calc for $C_4H_7CaO_3.2H_2O$: C, 34.0; H, 6.4.

2.5.4. Magnesium Gamma Hydroxybutyrate

$Mg(OH)_2$ (7.6 g, 0.125 moles) was suspended in water (25 mL) and then GBL (20mL, 0.26 moles) was added slowly in 5 mL portions. This was then heated for 1 h at 60-65 ^oC. Methanol (37.5 mL) was added to the cooled solution and it was left for 12 h before filtering through a Büchner funnel. The filtrate was then mixed with acetone (20 mL) and allowed to stand for 10 mins after which time a precipitate had formed. The solvent was decanted and then a further portion of acetone (20 mL) was added and the solvent again decanted. This stage was repeated once more. The product was then allowed to dry for 48 h at room temperature to afford $Mg(GHB)_2.3H_2O$ (32.4 g, 91%). Found: C, 34.0; H, 7.1. $C_4H_7MgO_3.3H_2O$: C, 33.9; H, 7.1.

2.6. Presumptive tests

Smiths reagent and chlorophenol red and modified Schweppes reagent were prepared by literature methods [15, 16].

2.7. Microcrystalline tests

The nitrate reagents were all prepared as 10 mg/mL aqueous solutions. The compounds; NaGHB, KGHB, $Mg(GHB)_2.3H_2O$ and $Ca(GHB)_2.2H_2O$ were made into solution at a concentration of 125 mg/mL. NaGHB underwent further serial dilution in preparation for further experiments with concentrations ranging from between 2 mg/mL to 125 mg/mL prepared and tested against the silver nitrate reagent which maintained its concentration of 10 mg/mL (1.0% w/v). All experiments were carried out using standard microscope slides (Thermo scientific. Menzel-gläser) which were used as received. 10 µL of each of the four GHB salts in aqueous solution were placed on individual glass microscope slides and then 10 µL of each of the nitrate standard reagents in aqueous solution was applied. All of the slides were allowed to dry at room temperature.

2.8. Microscopy and images

A Biolux AL 20x-1280x Biology Microscope with VGA Camera (Upper and lower illumination: LED light source) was used to obtain VGA images of the results. A

standard desktop PC utilising ArcSoft Photoimpression Software was used to obtain and record images.

3. Results and discussion

3.1. Synthesis and FT-IR spectroscopy

NaGHB was the most readily synthesised GHB salt. Sodium hydroxide was dissolved in ethanol and upon addition of GBL the product formed as a white precipitate that was collected and dried. As previously reported it was found that conditions such as increased temperature and more basic pH greatly affect the reaction of GBL, its hydrolysis and subsequent conversion to GHB [20]. Syntheses as well as analytical and microcrystal analysis of the four GHB salts was undertaken a number of times to ensure reproducibility of results. KGHB was found to be more soluble in ethanol and so diethylether was added to precipitate the product. Ca and Mg hydroxides are insoluble in ethanol so the syntheses were performed in water. In this solvent the group 2 salt precipitates are finely divided and move like opalescent liquid suspensions from which residual methanol, water and organic impurities could be removed by addition of acetone, mixing and then decanting the acetone. Group 2 salts prepared by this method without drying in an oven are non-hygroscopic, but retain waters of crystallisation. Elemental analysis suggests formulations of $Ca(GHB)_2.2H_2O$ and $Mg(GHB)_2.3H_2O$ supported by the presence of water peaks (ca. 3100 cm^{-1}) in their IR spectra (Table 1). The spectrum of $Ca(GHB)_2.2H_2O$ is very similar to that previously reported [21] and the spectrum of $Mg(GHB)_2.3H_2O$ which is shown in Figure 1. The IR spectra of NaGHB and KGHB are very similar to each other and to those published previously [21]. The most characteristic peaks are those assigned to the carboxylate stretch in the region 1544-1557 cm^{-1}. The hygroscopic nature of the group 1 salts is revealed in the IR spectra as recording a freshly dried sample shows considerably less water peaks and sharper absorptions compared with an older sample. It is possible to obtain elemental analysis data from carefully stored Na and K salts which show no significant levels of hydration.

Table 1

FT-IR spectroscopic data

NaGHB (cm^{-1})	KGHB (cm^{-1})	$Mg(GHB)_2.3H_2O$ (cm^{-1})	$Ca(GHB)_2.2H_2O$ (cm^{-1})

		410 m	427 w
		462 m	462 m
482 m	482 m		493 m
549 m	549 m	542 m	533 m
576 w	576 w		
		612 m	611 m
635 m	636 m		
662 m	663 m	675 w	664 m
751 w	751 w	759 m	750 m
			808 m
869 w	868 w	873 m	868 w
881 w	881 w		
		903 w	909 w
920 m	920 m		
		930 w	936 m
946 w	946 w		
		991 m	
1014 s	1014 s	1021 s	
		1034 s	1032 s
1052 m	1052 m		
1066 m	1066 m	1070 w	1065 w
		1085 m	1080 m
1157 w	1156 w	1168 m	
			1199 w
1228 w	1228 w	1231 m	1237 w
1272 w	1272 w		1273 w
		1290 s	
		1305 m	1302 m
		1318 w	1313 s
1328 m	1328 m		
1361 m	1361 m		
1385 m	1385 m		
1406 s	1406 s	1398 s	1404 s
1449 m	1448 m	1448 w	1448 m
			1471 w
1557 m	1557 m	1556 s	1544 s
			1584 m
		1651 w	
		1693 w	
		1769 w	
2872 w	2875 w	2838 w	2833 w
2944 w	2944 w	2973 w	2941 w
2960 w	2960 w		
		3108 m	3089 w br

3301 m	3304 m	3275 m	

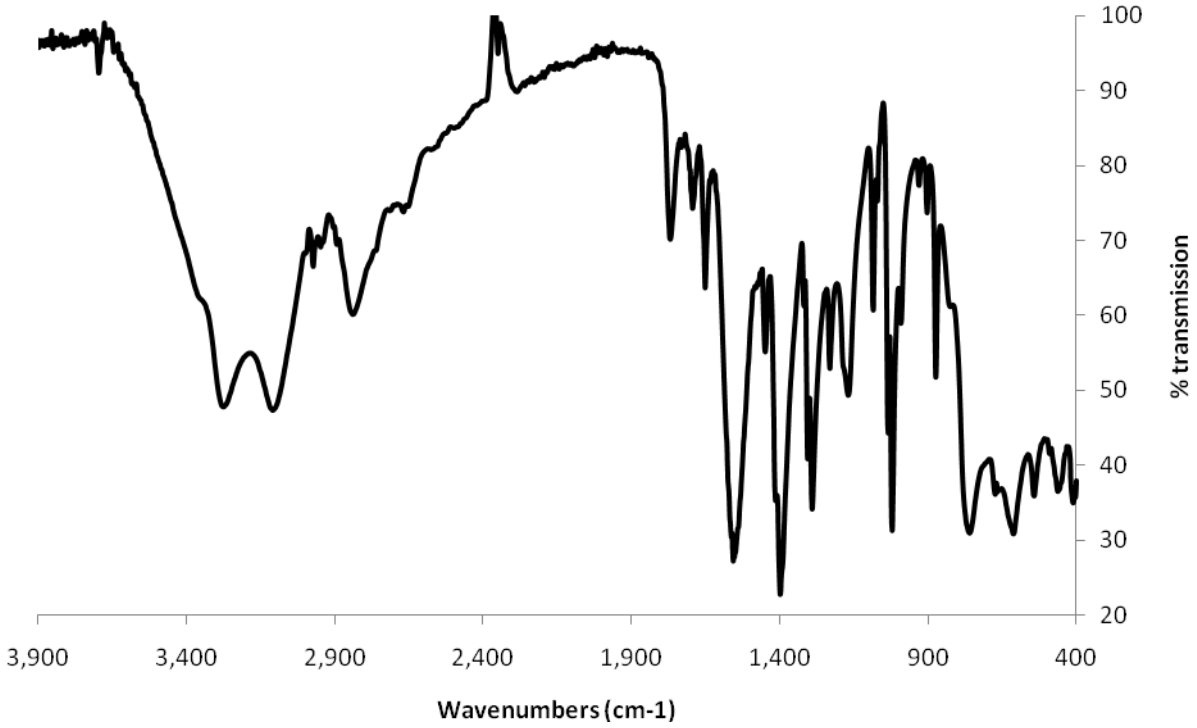

Fig. 1. FT-IR spectrum of $Mg(GHB)_2.3H_2O$

3.2. Presumptive Tests

The Smith test is a colour change test which indicates a positive result when the colour of the solution changes from a deep orange colour to a dark green colour. The method used to synthesise the Smith test solution was followed from the Virginia Department of Forensic Science [15]. The four salts of GHB all tested positive. A second test mixture of chlorophenol red and modified Schweppes reagent in a 3:1 ratio was investigated [16]. In a positive result for GHB the solution changes from a light orange colour to a dark red colour. Again all four GHB salts gave positive results.

3.3. Microcrystalline Tests

Each of the compounds was placed in to aqueous solution at a concentration of 125 mg per mL. This is much higher than doses that would normally be found or taken by

persons knowingly or otherwise. A high concentration was used so that the suitability of any of the nitrates to be an identifiable crystal forming reagent with any of the salts could be established. All experiments were undertaken at least three times.

Table 2 Results of the microcrystalline tests

Nitrate	NaGHB	KGHB	$Mg(GHB)_2.3H_2O$	$Ca(GHB)_2.2H_2O$
$AgNO_3$	Rectangular right angled crystals	Crystals	NC	NC
$NaNO_3$	NC	GC	NC	NC
$Ba(NO_3)_2$	NC	NC	NC	NC
$Ca(NO_3)_2$	NC	NC	GC	NC
$Co(NO_3)_2$	RC	GC	NC	RC
$Cu(NO_3)_2$	NC	GC	GC	NC
$Mn(NO_3)_2$	NC	NC	NC	NC
$Ni(NO_3)_2$	NC	GC	NC	NC
$Zn(NO_3)_2$	NC	GC	NC	NC
$Fe(NO_3)_3$	NC	NC	NC	NC
$La(NO_3)_3$	NC	NC	NC	GC
$Tl(NO_3)_3$	NC	NC	NC	NC
$Y(NO_3)_3$	NC	RC	NC	RC
$Zr(NO_3)_4$	NC	GC	GC	NC
$Ba(NO_3)_2$ & $AgNO_3$	Rectangular very small crystals	NC	NC	NC
$Ca(NO_3)_2$ & $AgNO_3$	Partially rectangular clumped crystals	NC	NC	NC
$Co(NO_3)_2$ & $AgNO_3$	Small rectangular crystals	NC	NC	NC
$Cu(NO_3)_2$ & $AgNO_3$	Few rectangular crystals	NC	NC	NC
$Fe(NO_3)_3$ & $AgNO_3$	Long rectangular crystals	GC	NC	NC
$La(NO_3)_3$ & $AgNO_3$	Larger crystals, defined shape	RC	NC	NC
$Mn(NO_3)_2$ & $AgNO_3$	Many thorn shaped crystals	NC	NC	NC
$Ni(NO_3)_2$ & $AgNO_3$	Few rectangular crystals, mostly deformed	NC	NC	NC
$NaNO_3$ & $AgNO_3$	Few crystals at edge of sample	NC	NC	NC

$Tl(NO_3)_3$ & $AgNO_3$	Few rectangular crystals, and sharp edged crystals	NC	NC	NC
$Y(NO_3)_3$ & $AgNO_3$	Rectangular, sharp edged and deformed crystals	NC	NC	NC
$Zn(NO_3)_2$ & $AgNO_3$	Rectangular, sharp edged and deformed crystals	NC	NC	NC
$Zr(NO_3)_4$ & $AgNO_3$	Few disfigured, aggregated crystals	NC	NC	NC

NC no crystals, RC reagent crystals, GC crystals of the GHB salt being tested.

3.3.1. NaGHB

In the present work it was found that NaGHB and $AgNO_3$ formed distinctive rectangular crystals (Table 2). A previous report suggested that a combination of $AgNO_3$ and $Cu(NO_3)_2$ is required to form the crystals [17]. Crystal formation does occur with Na-GHB and $AgNO_3/Cu(NO_3)_2$, however crystal formation will occur without $Cu(NO_3)_2$ and with just $AgNO_3$ alone and it has been suggested that this may be related to different methods of reagent preparation [18]. The results were in agreement with previous work that out of the 15 nitrate reagents tested, $AgNO_3$ is the only nitrate that produces right angled crystals when tested with NaGHB [19]. It was further determined that when $AgNO_3$ was coupled with a range of 14 other nitrates crystals would form in all cases. However the crystals changed in appearance and size. Some of the nitrates coupled would disfigure the crystals formed significantly in particularly $Ni(NO_3)_2$ and $Zn(NO_3)_2$. In the case of coupling $AgNO_3$ with $La(NO_3)_3$ it was found as previously reported that right angled crystals formed with NaGHB that were larger in size but still had the same characteristics as the crystals formed with $AgNO_3$ [19].

A range of concentrations of Na-GHB were tested with $AgNO_3$ and $AgNO_3$+$La(NO_3)_3$ from 2 mg/mL to 125 mg/mL and in all cases positive results were obtained. The concentration of NaGHB did not affect time taken for the crystals to form and crystal formation can be observed after ~3 minutes at 22 ^oC. Crystal size varies but is typically in the range 10-245 µm. Time is critical when observing and identifying the crystals as clumping and aggregation occurs upon complete drying.

3.3.2. KGHB

In the case of KGHB, there was crystal formation with the $AgNO_3$ reagent. The K-GHB derived crystals are thin and in the majority of cases somewhat curved. The crystals formed are not comparable to the crystals formed from Na-GHB and $AgNO_3$ in either shape or size. There was also formation of long thick crystals with $Co(NO_3)_2$, $Cu(NO_3)_2$, $Ni(NO_3)_2$ and $NaNO_3$ which were indistinguishable from crystals formed by allowing K-GHB to dry on its own. Elongated reagent crystals were observed to form when $Y(NO_3)_3$ was tested with K-GHB. Thorn shaped crystals indistinguishable from K-GHB were observed to form with $Zn(NO_3)_2$, $Zr(NO_3)_4$ and the coupled reagent $Fe(NO_3)_3$+$AgNO_3$. Needle like crystals were observed to form between the coupled $La(NO_3)_3$+$AgNO_3$ and K-GHB. These crystals were similar to $La(NO_3)_3$ and not a reliable indication of the presence of K-GHB.

3.3.3. $Mg(GHB)_2.3H_2O$

In the case of $Mg(GHB)_2.3H_2O$, there was no crystal formation with the $AgNO_3$ reagent. Crystals formed when $Mg(GHB)_2.3H_2O$ was tested with $Ca(NO_3)_2$, $Cu(NO_3)_2$ and $Zr(NO_3)_4$, but the crystals appeared to be merely the dry crystallised form of $Mg(GHB)_2.3H_2O$.

3.3.4. $Ca(GHB)_2.2H_2O$

In the case of $Ca(GHB)_2.2H_2O$ there was no crystal formation with the $AgNO_3$ reagent. However needle like crystals formed with $Y(NO_3)_3$ and $La(NO_3)_3$ which were similar in appearance to $Ca(GHB)_2.2H_2O$. Aggregated crystals were observed to form when $Ca(GHB)_2.2H_2O$ was tested with the $Co(NO_3)_2$, however these were indistinguishable from the dried $Co(NO_3)_2$ reagent.

3.4. X-ray powder diffraction

To further characterise the materials and also offer a non-destructive method of identification X-ray powder diffraction patterns were recorded. The GHB salts were homogenised and the diffraction patterns recorded on several samples to confirm homogeneity. Representative diffraction patterns are presented with their intensities

normalised for ease of comparison (Figure 2) and the major peaks in each pattern are tabulated (Table 3).

For NaGHB the largest peak is at the start of the pattern at 6.13 degrees 2-theta and suggests that the structure has a layered periodicity with a gap between the layers of approximately 14.3 Å. For KGHB the low number of counts reflected in the higher noise in Figure 2 show that it is poorly crystalline and the deviation away from the baseline indicate that it also contains an amorphous phase. Again there is a large peak at the start of the pattern which could be due to a layered phase with a periodicity of approximately 8.18 Å. This is unexpected given the larger nature of the potassium cation compared with sodium and suggests a different structural form.

The X-ray powder diffraction pattern of $Mg(GHB)_2.3H_2O$ contains a large number of peaks suggesting that it is a multi phase material and it does not appear to contain the same type of layer structure. It also appears to contain some amorphous material. The diffraction pattern of $Ca(GHB)_2.2H_2O$ was the only one to give a potential match on the JCPDS database which indicates that the material contains small amounts of calcite ($CaCO_3$). This intense peak has a d-spacing of 9.51Å. $Ca(GHB)_2.2H_2O$ potentially has structure similar to that found in the NaGHB and KGHB, however it also contains secondary phases.

In summary it appears that the Na, K and Ca salts contain a similar phase which could be a layered phase. NaGHB appears to be essentially phase pure whilst the KGHB and $Ca(GHB)_2.2H_2O$ materials also contain secondary phases. $Mg(GHB)_2.3H_2O$ however appears to be a complex mix of many phases and does not appear to contain the layered phase exhibited by the other materials. All four materials are clearly distinguishable by this non-destructive technique.

Table 3

Major peaks in the X-ray powder diffraction patterns

NaGHB Degrees 2Θ	KGHB Degrees 2Θ	$Mg(GHB)_2.3H_2O$ Degrees 2Θ	$Ca(GHB)_2.2H_2O$ Degrees 2Θ
6.16	10.82	12.26	9.32
12.32	18.18	13.53	10.88
23.92	21.14	13.98	14.18
24.82	21.60	15.52	14.44
30.04	23.34	16.30	18.60
31.20	25.76	17.08	21.36
34.22	28.32	19.46	23.00
35.64	29.74	20.06	23.56
36.14	31.64	20.84	23.88
37.64	31.98	21.94	25.12
41.48	39.46	22.78	27.92
43.00	40.48	24.56	28.44
47.66		25.42	29.04
48.50		26.36	29.92
		27.20	29.98
		28.10	35.46
		30.44	37.74
		31.25	38.42
		32.22	39.06
		34.46	39.54
		35.08	43.48
		35.68	44.18
		36.32	47.62
		37.22	57.84
		37.70	
		38.68	
		40.00	
		40.54	
		42.42	
		43.28	
		46.38	
		47.64	
		48.45	
		49.30	
		52.12	

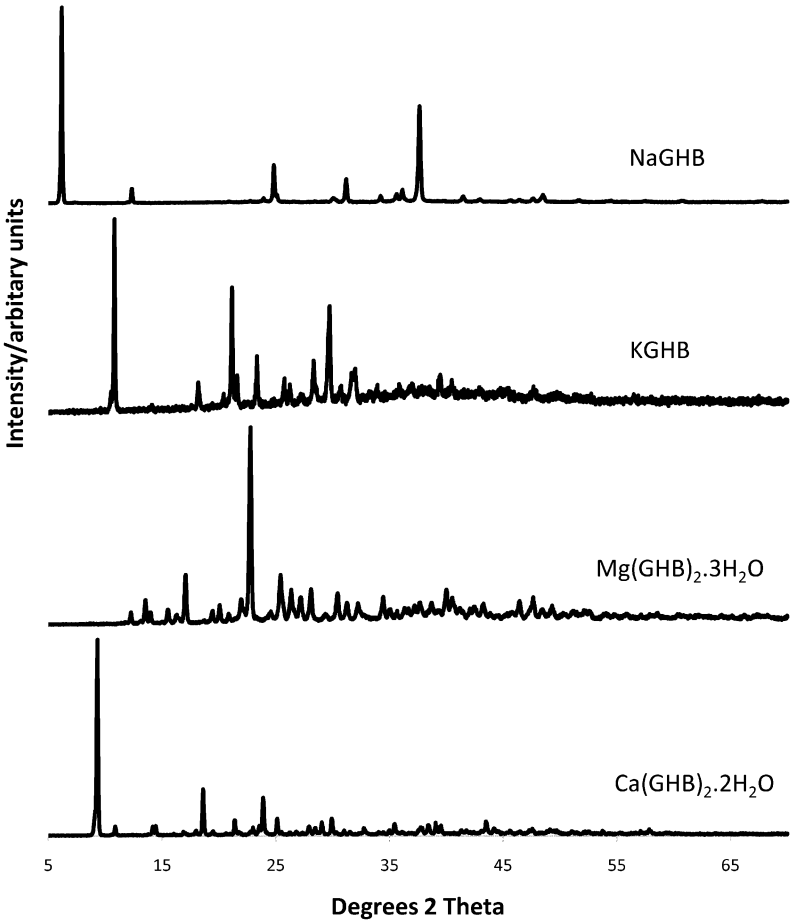

Fig. 2. X-Ray powder diffraction patterns of the GHB salts

4. Conclusions

The present work indicates that $AgNO_3$ cannot be used a confirmatory test for all GHB salts. In particular crystals were not obtained with the Group 2 salts. However it is known that AgGHB can be formed from $Ca(GHB)_2$ and $AgNO_3$ in the bulk [21] and possibly the conditions could be optimised to allow crystal formation [22].

X-Ray powder diffraction shows great promise for the quick, non-destructive identification of bulk samples. When a forensic drug laboratory is assigned a sample to identify whether it contains GHB or GBL it would be more accurate to report the actual salt form of the GHB found. The X-Ray powder analysis of GHB in its salt form can establish the reagent used in its manufacture. Establishing a link between a GHB salt and the reagents used during its synthesis found at a suspect's premise may provide important information during an investigation.

Although the evidential requirements for various convictions related to GHB offenses require only the GHB itself and not its salt form, the identification of the salt form may be useful. It may be possible to use the information gained regarding the salt form of GHB to establish the origin and batch similarities.

Acknowledgements

We are grateful to Dr D.C. Arnold for help with interpreting the X-ray powder diffraction patterns.

References

[1] J.A. Siegel, Forensic Identification of Illicit Drugs, in: R. Saferstein (Ed), Forensic Science Handbook, Volume 2, Pearson International, 2005, pp. 112-174.

[2] http://homeoffice.gov.uk/drugs/drug-law/. Accessed 26/8/11

[3] http://homeoffice.gov.uk/about-us/corporate-publications-strategy/home-office-circulars/circulars-2011/005-2011/. Accessed 26/8/11

[4] C.S. Marvel, E.R. Birkhimer, Preparation of the Sodium Salts of Omega-Hydroxybutyric, -Valeric and -Caproic Acids, J. Am. Chem. Soc. 51 (1929) 260-262.

[5] H. Laborit, Mechanisms of Orientation of Metabolic Pathways as a Function of Environment and Pharmacological Agents, Agressologie. 2 (1961) 439–460.

[6] L.P. Carter, D. Pardi, J. Gorsline, R.R. Griffiths, Illicit Gamma-hydroxybutyrate (GHB) and Pharmaceutical Sodium Oxybate (Xyrem®): Differences in Characteristics and Misuse, Drug and Alcohol Dependence, 104 (2009) 1-10.

[7] http://www.scribd.com/doc/36299006/GHB-Synthesis-1. Accessed 7/6/11

[8] http://timestream.org/ghb/patent.html. Accessed 7/6/11

[9] L. Walker, Identification of the Potassium Salt of Gamma-hydroxybutyric Acid (GHB), J. Clandestine Laboratory Investigating Chemists Association. 9 (1999) 17.

[10] J.S. Chappell, A.W. Meyn, K.K. Ngim, The Extraction and Infrared Identification of Gamma-Hydroxybutyric Acid (GHB) from Aqueous Solutions, J. Forensic Sci. 49 (2004) 1-8.

[11] S.L. Chew, J.A. Meyers, Identification and Quantification of Gamma-Hydroxybutyrate (NaGHB) by Nuclear Magnetic Resonance Spectroscopy, J. Forensic Sci. 48 (2003) 1-7.

[12] J.V. DeFrancesco, M.R. Witkowski, L.A. Ciolino, GHB Free Acid: I. Solution Formation Studies and Spectroscopic Characterization by ^{1}H NMR and FT-IR, J. Forensic Sci. 51 (2006) 321-329.

[13] M.R. Witkowski, L.A. Ciolino, J.J. DeFrancesco, GHB Free Acid: II. Isolation and Spectroscopic Characterization for Forensic Analysis, J. Forensic Sci. 51 (2006) 330-339.

[14] A.G. Del Signore, M. McGregor, B.P. Cho, ^{1}H NMR Analysis of GHB and GBL: Further Findings on the Interconversion and a Preliminary Report on the Analysis of GHB in Serum and Urine, J. Forensic Sci. 50 (2005) 1-6.

[15] Virginia Department of Forensic Science. Controlled Substances Procedures Manual. http://www.dfs.virginia.gov/manuals/controlledSubstances/procedures/221-D100%20Controlled%20Substances%20Procedures%20Manual.pdf. Accessed 7/6/11.

[16] A.C. Moffat, B. Widdop, M. D. Osselton, Clarke's Analysis of Drugs and Poisons. Pharmaceutical Press 3rd Edition, 2004.

[17] K.M. Andrea, H.K. Evans, C.M. Wojcikn, Microcrystal Identification of Gamma-Hydroxybutyrate (GHB), J. Forensic Sci. 45 (2004) 665-668.

[18] S.C. Bell, L.S. Oldfield, D.M. Shakleya, J.L. Peterson, J.W. Mercer, Chemical Composition and Structure of the Microcrystals Formed Between Silver (I) and γ-Hydroxybutyric Acid and γ-Hydroxyvaleric Acid, J. Forensic Sci. 51 (2006) 808-811.

[19] M.P. Elie, M.G. Baron, J.W. Birkett, Enhancement of Microcrystalline Identification of γ-Hydroxybutyrate, J. Forensic Sci. 53 (2008) 147-150.

[20] L.A. Ciolino, M.Z. Mesmer, R.D. Satzger, A.C Machal, H.A. McCauley, A.S. Mohrhaus, The Chemical Interconversion of GHB and GBL: Forensic Issues and Implications. J. Forensic Sci. 46 (2001) 1315-1323.

[21] J.V. DeFrancesco, Gamma-Hydroxybutyrate, Silver Salt (AgGHB): Identification of gamma-Hydroxybutyrate (GHB) via Conversion to the Silver Salt, Microgram Journal, 3 (2005) 46-53.

[22] M.G. Barton. Personal communication.