Bupropion

Background (e.g. history, therapeutic use, abuse, effects):

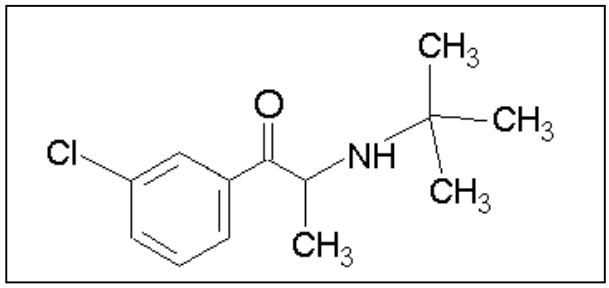
Historically, bupropion (amfebutamone) has been available in the U.S. as an antidepressant (Wellbutrin®). It is structurally unrelated to other antidepressants but has a therapeutic efficacy similar to tricyclic antidepressants. However, it has recently been prescribed in the U.K. as a smoking cessation adjunct (Zyban®). It is not prescribed in the U.K. as an antidepressant.

There have been no reported instances of abuse of the drug in the U.K. but it is structurally similar to the phenylethylamines and therefore may result in various analytical problems e.g. false positive amphetamine results using immunoassay.

Although the neurochemical effect of bupropion is not completely understood, there is evidence that it may block dopamine re-uptake and block serotonin and noradenaline uptake. It does not appear to inhibit monoamine oxidase.

Chemical Data

Structure:



Chemical name:
1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)-amino]-1-propanone

Chemical formula and weight:
239.74 (weight)

CAS number:
34911-55-2

Metabolism and Pharmacokinetics

Bupropion is extensively metabolised by hydroxylation and reduction to form 3 less active major metabolites; (I) morpholinol metabolite (hydroxybupropion) (II) erythroamino alcohol metabolite and (III) threoamino alcohol metabolite.

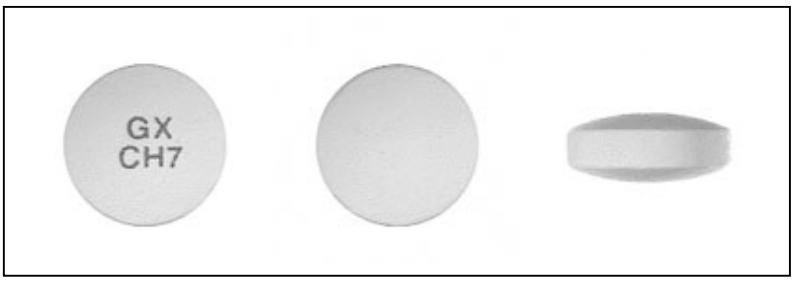
The 3 metabolites all have longer half-lives than the parent drug and less than 0.5% of a single dose is excreted unchanged in urine. The plasma half-life appears to be approximately 14 hours. There is also some published data regarding storage of bupropion stored in plasma at high temperatures (half-life at 22^{o}C = 54 hours, at 37^{o}C = 11 hours). There appeared to be no effect on the stability of the major metabolites.

Toxicity (including non-fatal and fatal data)
There are limited published data regarding toxicity and resulting blood concentrations, however, it has been reported that following ingestion of a single 100 mg dose, an in life peak plasma bupropion concentration of 0.14 mg/L was attained.
In overdose, toxic effects have been noted to be anxiety, tremor and tachycardia. In five U.S. cases of fatalities involving bupropion, post mortem blood concentrations of 4.0 mg/L (unspecified site), 0.16 mg/L (unspecified site), 4.2 mg/L (unspecified site), 11.0 mg/L (femoral) and 13.0 mg/L (subclavian). In one U.K. case of death involving suspected bupropion overdose a post mortem blood concentration of 5.7 mg/L (femoral) was measured.

Proprietary preparations
Wellbutrin (USA)
Zyban (UK)

Dosage
In the U.K. bupropion is usually prescribed initially at 150 mg three times a day, followed by a reduction to 150 mg twice a day.

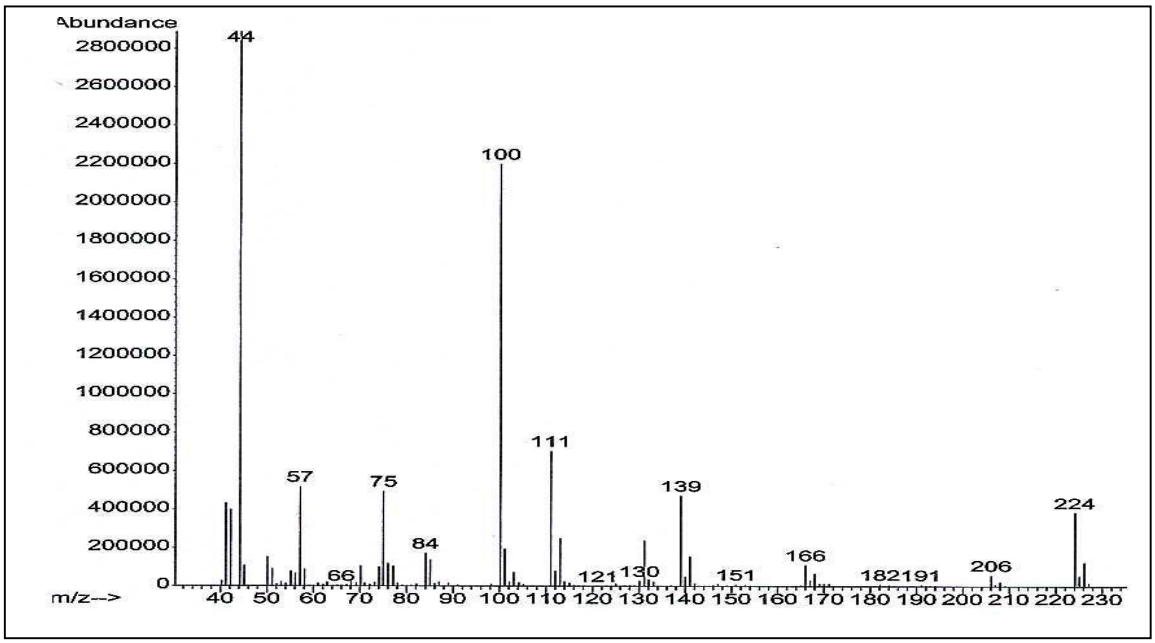
Tablet
Zyban (bupropion HCl)



Size: Diameter (mm) = not specified Height (mm) = not specified
Weight (mg): 150 mg

Analytical Data

GC-MS mass-spectrum
Bupropion (underivatised)



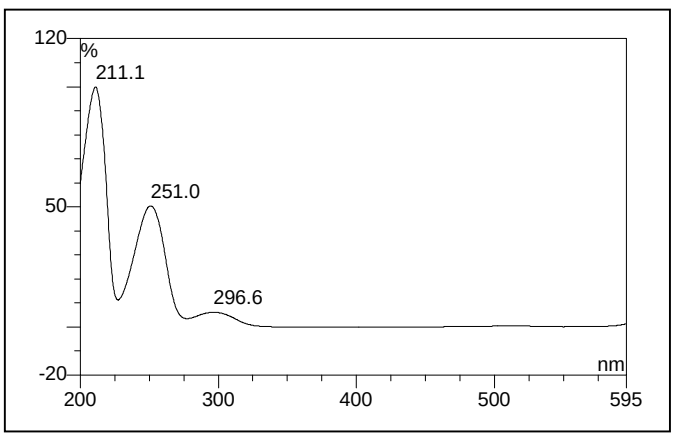
LC-MS mass-spectrum
Not available

GC elution data
Elutes between illicit drugs BDB and MBDB on DB-5 column. Parent bupropion and all metabolites are separated.

HPLC elution data
OD/CN column = co-elution of parent compound and one metabolite (MeCN and water 0-70% ramp)

"Silica column" (e.g. ODS) = separation of parent and metabolites

UV spectrum
Bupropion



Immunoassay data

EMIT amphetamine assay = ?cross-reaction

CEDIA amphetamine assay = >18 mg/L in urine gives positive result

Monograph produced by
Simon Elliott, Regional Laboratory for Toxicology, City Hospital NHS Trust, Birmingham, U.K.

References

Martindale – The Extra Pharmacopoeia, 30th Ed. Ed. James Reynolds, Pharmaceutical Press, 1993, page 250.

R. C. Baselt, "Bupropion" in Disposition of toxic drugs and chemicals in man (5th Ed.), 2000.

P. N. Friel et al, “Three fatal drug overdoses involving bupropion”, J. Anal. Tox., vol 17, 1993, pages 436-438.

T. A. Jennison et al, “A HPLC method for quantitating bupropion in human plasma and serum”, J. Anal. Tox., vol 19, 1995, pages 69-72.

T. A. Rohrig and N. G. Ray, “Tissue distribution of bupropion in a fatal overdose”, J. Anal. Tox., vol 16, 1992, pages 343-345.

S. P. Elliott, unpublished findings in a fatality involving bupropion, 2001.

S. C. Laizure and C. L. DeVane, “Stability of bupropion and its major metabolites in human plasma”, Ther. Drug Monit., vol 7, 1985, pages 447-450.

N. Wohlenberg et al, “Postmortem quantitation of bupropion (Wellbutrin) in blood using the Finnigan Ion Trap Detector”, TIAFT Bulletin, vol 22 (4), 1992.

J. E. Meeker et al, “A suicidal overdose of bupropion (Wellbutrin)”, TIAFT Bulletin, vol 22 (4), 1992.