= Benzylpiperazine =

Benzylpiperazine (BZP) is a recreational drug with euphoriant and stimulant properties . The effects produced by BZP are comparable to those produced by amphetamine . Adverse effects have been reported following its use including acute psychosis , renal toxicity and seizures . No deaths have been reported following a sole ingestion of BZP , although there have been at least two deaths from the combination of BZP and MDMA . Its sale is banned in several countries , including Australia , Canada , New Zealand , the United States , the Republic of Ireland , the United Kingdom , Bulgaria , Romania and other parts of Europe .

= = History = =

= = = Development history = = =

It is often claimed that BZP was originally synthesized as a potential antihelminthic (anti @-@ parasitic) agent for use in farm animals . However , there are some references to BZP in medical literature that predate interest in piperazines as antihelminthics . Even so , the majority of the early work with the piperazines were investigations into their potential use as antihelminthics with the earliest clinical trials in the literature relating to piperazine being articles in the British Medical Journal in the 1950s . It was discovered that BZP had side effects and was largely abandoned as a worm treatment . It next appears in the literature in the 1970s when it was investigated as a potential antidepressant medication , but rejected when research reported that BZP had amphetamine @-@ like effects and was liable to abuse . The study suggested that BZP ? should be placed under statutory control similar to those regulating the use of amphetamine . ?

= = = Recreational history = = =

In the early 1990s , the United States Drug Enforcement Administration noted the drug was being used recreationally in California . It also reported that BZP was being used as an adulterant in illicit drugs . Not long after , there was an explosion in the drug 's use worldwide ? a situation which was soon followed by legislative control in many countries . Since 1999 , benzylpiperazine use grew sharply in New Zealand due to an initial complete lack of regulation . The New Zealand government attempted to ban the product as of 18 December 2007 , but the necessary second reading of the bill did not happen in time for the law to be passed . It was so widely used that an estimated 5 million pills were sold in New Zealand in 2007 . Piperazine @-@ based stimulants began to appear in Europe in 2000 but remained virtually unavailable in the rest of the world until recently . In early 2006 , pills containing the active ingredients BZP and TFMPP began to appear in the city of Vancouver , Canada , where they first gained popularity with late night party @-@ goers as a safer alternative to many of the illicit street drugs commonly available there . In 2007 piperazine based party @-@ pill formulations started to become widely available nationwide which has caused concern with local authorities such as Health Canada and subsequently BZP has gained much media attention in 2008 . As of May 2008 piperazines such as BZP and TFMPP have been under evaluation by Health Canada in order to determine whether or not party @-@ pills pose a significant health risk to individuals . At this time no official decision has been made regarding these specific piperazines becoming restricted substances , or if they should be banned altogether in Canada . In the United States , it is still used as an adulterant in ecstasy mimic tablets .

= = Production and distribution = =

BZP is a piperazine derivative which comes as either the hydrochloride salt or a free base . The hydrochloride salt is a white solid while the base form is a slightly yellowish @-@ green liquid . BZP base is corrosive and causes burns .

In countries where its purchase is legal , BZP products are often produced in small specialist laboratories . The raw materials can be purchased from various chemical supply agencies and formed into tablets or capsules using relatively cheap production techniques . The resulting product can be marketed at extremely high markup , so end @-@ user prices can be as high as 300 times the bulk cost of raw ingredients .

BZP is often marketed ostensibly as a " dietary supplement " to avoid meeting stricter laws that apply to medicines and drugs , despite the fact that BZP has no dietary value . As of late 2005 , the Misuse of Drugs Act ensured it can no longer be classified or marketed as a dietary supplement in New Zealand . Some retailers claim that BZP is a " natural " product , describing it as a " pepper extract " or " herbal high , " when in fact the drug is entirely synthetic , and has not been found to occur naturally .

= = Pharmacodynamics = =

BZP has been shown to have a mixed mechanism of action , acting on the serotonergic and dopaminergic receptor systems in a similar fashion to MDMA . BZP has amphetamine @-@ like actions on the serotonin reuptake transporter , which increase serotonin concentrations in the extracellular fluids surrounding the cell and thereby increasing activation of the surrounding serotonin receptors . BZP has a lower potency effect on the noradrenaline reuptake transporter and the dopamine reuptake transporter . BZP has a high affinity action at the alpha2 @-@ adrenoreceptor , it is an antagonist at the receptor , like yohimbine , which inhibits negative feedback , causing an increase in released noradrenaline .

BZP also acts as a non @-@ selective serotonin receptor agonist on a wide variety of serotonin receptors ; binding to 5HT2A receptors may explain its mild hallucinogenic effects at high doses , while partial agonist or antagonist effects at the 5HT2B receptors may explain some of BZPs peripheral side effects , as this receptor is expressed very densely in the gut , and binding to 5HT3 receptors may explain the common side effect of headaches , as this receptor is known to be involved in the development of migraine headaches .

= = Effects = =

The effects of BZP are largely similar to amphetamines , with one study finding that former amphetamine addicts were unable to distinguish between dextroamphetamine and BZP administered intravenously . Users report alertness , euphoria and a general feeling of well being . The perception of certain sensations such as taste , colour or music may be subjectively enhanced . The average duration is longer than that of dextroamphetamine , typically lasting 4 ? 6 hours with reports as long as 8 hours depending on the dose . A recent study has shown that mixtures of BZP with other piperazine drugs such as TFMPP share certain pharmacodynamic traits with MDMA .

= = = Subjective effects = = =

Upon ingestion of between 50 mg and 200 mg of BZP , the user may experience any or all of the following :

Initial Effects :

Feelings of euphoria , wonder , amazement , well @-@ being , energy and elation

Rapid mood elevation

Enhanced sociability

Enhanced appreciation of music

Increased desire to move , also slight increase in stereotypy

Skin tingling

Decreased appetite

Repetitive thought patterns

Actual and perceived changes in body temperature

Mild jaw clenching / bruxism
Increased heart rate
Dilation of pupils (see photo)
Nausea
Flushing
Mild xerostomia (dry mouth)
Slight urinary incontinence , often described as " leaking " a small amount of urine after urinating (not due to loss of bladder control)
Later Effects :
Mild headache
Nausea
Hangover @-@ like symptoms (common with high doses)
Fatigue
Indigestion (similar to acid indigestion / heartburn)
Increased hunger (and sometimes thirst)
Insomnia
Confusion
Depression (particularly with frequent / heavy use)

= = = Tolerance = = =

Research into BZP 's tolerance is sparse . Anecdotal evidence from online sources claim tolerance to the central action of BZP will develop quickly . Due to tiredness associated with the body 's recovery from stimulants , such as BZP , it is uncommon for users to be able to sustain a week @-@ long intake .

= = = Toxic effects = = =

As with most sympathomimetic stimulants there appear to be significant side effects associated with BZP use . BZP reportedly produces insomnia and a mild to severe hangover after the drug effect wears off , however , some manufacturers in New Zealand have started including recovery pills which contain 5 @-@ HTP and vitamins which allegedly ease these hangovers .
The major side effects include dilated pupils , blurred vision , dryness of the mouth , extreme alertness , pruritus , confusion , agitation , tremor , extrapyramidal symptoms (dystonia , akathisia) , headache , dizziness , anxiety , insomnia , vomiting , chest pain , hallucinations , paresthesia , tachycardia , hypertension , palpitations , collapse , hyperventilation , sweating , hyperthermia and problems with urine retention . The more severe toxic effects include psychosis or adverse psychiatric events , renal toxicity , respiratory failure , hyperthermia , serotonin syndrome , rhabdomyolysis and seizure . Blood benzylpiperazine concentrations have been measured either to confirm clinical intoxication or as part of a medicolegal death investigation .

= = = = Christchurch study = = = =

The majority of the toxic effects information came from a study conducted between 1 April 2005 to 1 September 2005 . The study recorded all presentations associated with party pill use at the Emergency Department of Christchurch Hospital , New Zealand by recording them on a prospective data collection form . The aim was to study the patterns of human toxicity related to the use of benzylpiperazine @-@ based ' party pills ' . 61 patients presented on 80 occasions . Patients with mild to moderate toxicity experienced symptoms such as insomnia , anxiety , nausea , vomiting , palpitations , dystonia and urinary retention . Significantly , fourteen toxic seizures were recorded with two patients suffering life @-@ threatening toxicity with status epilepticus and severe respiratory and metabolic acidosis . It was concluded that BZP appears to induce toxic seizures in neurologically normal subjects . The results of this study and others like it showed that BZP can

cause unpredictable and serious toxicity in some individuals , but the data and dosage collection were reliant on self reporting by drug users , which may result in under @-@ reporting (or over @-@ reporting) , and there were complicating factors like the frequent presence of alcohol and other drugs .

= = = Risk of fatality = = =

A retrospective study carried out at an Auckland emergency department found that BZP presentations only made a minor contribution to their overdose database with most cases not producing any significant toxicity . Several cases where BZP individually or combined with alcohol or other medicines or illicit drugs resulting in complications exist . One such example is the well publicised case of a combination of BZP and MDMA by a 23 @-@ year @-@ old from Greymouth , New Zealand . Ben Rodham , a DJ , ingested a combination of BZP and MDMA in February 2007 , which nearly resulted in his death . Rodham was put into an induced coma in an effort to prevent him from dying . He later recovered .

In a case in Zurich in 2001 a 23 @-@ year @-@ old who had taken BZP and ecstasy (MDMA) died from a massive cerebral edema 57 hours after hospital admission .

= = = Addictive effects = = =

One in every 45 (2 @.@ 2 %) last @-@ year users of BZP in New Zealand is classed as dependent upon it , although 97 @.@ 9 % of users said that " it would not be difficult to stop using legal party pills " , and 45 @.@ 2 % of people who reported using both BZP and illegal drugs such as methamphetamine reported that they used BZP so that they did not have to use methamphetamine , which was perceived as more harmful . Still , most of the people who use BZP , even though they say it is quite easy to stop , do not want to , and continue to use the drug , feeling that it helps them to reach higher levels of mood , sociability , and energy . Studies undertaken on animals have indicated that BZP can substitute for methamphetamine in addicted rats , although it is one @-@ tenth as potent and produces correspondingly weaker addictive effects .

= = Legal issues = =

The drug was classified as a Schedule I controlled substance in the United States in 2002 , following a report by the DEA which incorrectly stated that BZP was 10 to 20 times more potent than amphetamine , when in fact BZP is ten times less potent than dexamphetamine . BZP is banned in all Australian states . Victoria , the last state in which it was legal , changed its classification on 1 September 2006 . This is the date BZP and piperazine analogs become illegal in the federal schedules which are now enacted by all Australian states and territories . BZP is also a banned substance in Japan , along with TFMPP . Both Australia and Japan admit that their scheduling decisions were made primarily in response to the Schedule 1 classification given to BZP in the USA , although some instances of BZP use had been reported by law enforcement authorities in both countries . BZP is also banned in Greece , Poland , Italy , Ireland , Malta , Estonia , Denmark and Sweden .

In Canada , Benzylpiperazine and salts of benzylpiperazine are classified as Schedule III controlled substances under the Controlled Drugs and Substances Act .

Piperazine and salts of piperazine are classified as Prescription Only Medicines in the UK . Any products containing salts of piperazine would be licensable under the Medicines Act and consequently anyone manufacturing and supplying it legally must hold the relevant licenses to do so . BZP is not a salt of piperazine , but mislabelling of BZP products as containing " piperazine blend " resulted in some prosecutions of suppliers in the UK by the Medicines and Healthcare Products Regulatory Agency , although none were successful . In May 2009 , the Home Office announced plans to ban BZP , and launched a consultation on the proposal . In October 2009 , it was announced that from 23 December 2009 , BZP and related piperazines would be Class C drugs

under the Misuse Of Drugs Act .

BZP is not controlled under any UN convention , so the compounds themselves are legal throughout most of the world , although in most countries their use is restricted to pharmaceutical manufacturing and recreational use is unknown .

Benzylpiperazine is , however , to be the subject of a European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) risk assessment , the results of which may determine what , if any , control will placed on BZP throughout the European Union . The risk assessment comes about as the result of a joint Europol ? EMCDDA report which concluded that BZP needs to be looked at in more detail . The results were published in June 2007 . The report concluded that the use of BZP can lead to medical problems even if the long effects are still unknown . Taking this concession as a basis , the European Commission has decided to ask the Council to place BZP under control of the UN Convention on Psychotropic Substances . On 4 March 2008 , the EU requested countries to place BZP under control within a year and France complied in May 2008 .

Based on the recommendation of the EACD , the New Zealand government has passed legislation which placed BZP , along with the other piperazine derivatives TFMPP , mCPP , pFPP , MeOPP and MBZP , into Class C of the New Zealand Misuse of Drugs Act 1975 . A ban was intended to come into effect in New Zealand on 18 December 2007 , but the law change did not go through until the following year , and the sale of BZP and the other listed piperazines became illegal in New Zealand as of 1 April 2008 . An amnesty for possession and usage of these drugs was in effect until October 2008 , at which point they became completely illegal .

= = Chemical derivatives = =

Pharmaceuticals
Befuraline ? Antidepressant
Bifeprunox ? Antipsychotic
Buclizine ? Antihistamine
Chlorbenzoxamine ? Gastrointestinal agent
Fipexide ? Nootropic
Imatinib ? Anticancer agent
Meclozine ? Antihistamine
Piberaline ? Antidepressant
Piribedil ? Antiparkinsonian agent
Trimetazidine ? Antianginal
Vesnarinone ? Cardiotonic
Designer drugs
4 @-@ Acetyl @-@ 1 @-@ benzylpiperazine (AcBZP , AceticBenzylPiperazine)
4 @-@ Methyl @-@ 1 @-@ benzylpiperazine (MBZP)
4 @-@ Bromo @-@ 2 @,@ 5 @-@ dimethoxy @-@ 1 @-@ benzylpiperazine (2C @-@ B @-@ BZP)
1 @,@ 4 @-@ Dibenzylpiperazine (DBZP)
3 @,@ 4 @-@ Methylenedioxy @-@ 1 @-@ benzylpiperazine (MDBZP)
Befuraline , fipexide , and piberaline are all known to metabolize to BZP .
All diphenylmethylpiperazines are also technically benzylpiperazines .