

Research Article

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Bromo-DragonFly: Chemistry, Pharmacology and Toxicology of a Benzodifuran Derivative Producing LSD-Like Effects

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Abstract

Bromo-DragonFly is a potent and long-acting psychedelic drug producing both LSD-like effects and amphetamine activation. This drug appeared within the recreational drug market in the early 2000s, since then, many cases of severe intoxication and fatalities related with its consumption have been signalled in some countries. The aim of this paper is to summarize the clinical, pharmacological and toxicological information currently available about this new and dangerous hallucinogenic substance of abuse.

Keywords: Bromo-DragonFly; Bromo-benzodifuranil-isopropylamine; Spamfly; Fly-compounds; Phenethylamines

Introduction

In the last decades, the spread of psychotropic drugs belonging to the phenethylamine family has been continually on the rise [1,2]. These drugs are often synthesized illegally in underground laboratories or marketed via-internet by smart shops and chemicals research suppliers [1,3]. Recently, a phenethylamine-related compound named Bromo-DragonFly (BDF) has received large popularity among young people for its LSD-like effects [4]. BDF is a potent and long-acting synthetic psychedelic substance used as recreational drug since 2001 [4]. This drug, also called ABDF, FLY, DOB-Dragonfly, spamfly, placid, B-fly, 3C-Bromo-Dragonfly, bromo-benzodifuranil-isopropylamine, was first synthesized by Matthew A. Parker in the laboratory of David E. Nichols at Purdue University in 1998 as a new research probe to investigate central nervous system (CNS) serotonin receptor structure and activity [5]. The name of BDF is derived from a resemblance between its molecular skeleton and a dragonfly for the presence of two furan rings on opposing sides of a central phenyl ring forming the wings (Figure 1). No epidemiological study has investigated the spread of BDF among people, but since its appearance within the recreational drug market, several cases of severe intoxication and deaths have been related with its consumption in some countries [3,4,6-10]. Furthermore, 1230 and 7600 blotters of BDF have been seized in Finland in 2009 and 2010, respectively [11]. In addition, the discussion about this hallucinogen among drug users is still lively within the drugs forum [12-16]. Finally, the use of Google Insights for Search, a google application for compare search volume patterns across specific regions, categories, time frames and properties, has shown a shift of interest for this drug from Europe to North America in recent years [17]. Despite being considered a substance that causes concern in terms of its potency and toxicity [9], there is very little information about its acute and chronic

human toxicity. The aim of this paper is to summarize the clinical, pharmacological and toxicological information currently available about this new and dangerous hallucinogenic substance of abuse.

Methods

Literature searches were performed using the following electronic databases: PubMed, Embase, PsycINFO, Cochrane database, TOXNET, and Medscape. The keywords used were: Bromo-DragonFly, ABDF, FLY, DOB-Dragonfly, spamfly, placid, B-fly, 3C-Bromo-Dragonfly, bromo-benzodifuranil-isopropylamine. Furthermore, considering the paucity of formal scientific articles and in order to conduct a research of data as extensively as possible, the results were integrated with all the relevant information available within the unconventional references such as drugs forum, web-journals, and chemicals databases. Unconventional references were carried out using google search engine and were considered relevant for our work all reports or self experiences that described psychotropic effects, side effects, modality of consumption, and trend of misuse related with the consumption of BDF. No restriction in language was used in our research.

Chemistry

BDF, IUPAC name 1-(8-bromobenzo [1,2-b;4,5-b']difuran-4-yl)-2-aminopropane, is a phenethylamine-related compound belonging to the benzodifuran class [18]. This substance, molecular formula C₁₃H₁₂BrNO₂, is generally available as a pink or white crystalline powder. The free base has a molecular weight of 294.14389 g/mol and a melting point of over 240°C. BDF is generally supplied by manufacturers as a water-soluble hydrochloride salt showing a molecular weight of 330.61 g/mol [18-20]. Furthermore, the product used for recreational purpose is also marketed as liquid formulation, in the form of impregnated paper and in tablets [7,18].

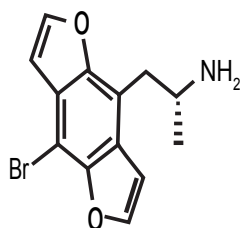


Figure 1: Bromodragonfly.

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Pharmacology

Studies in vitro and in animal models have shown that BDF is the most potent of the dihydrobenzofuran analogues with high affinity binding to the 5HT_{2A} receptor [5,19]. BDF exists in two stereoisomeric forms R and S, and R-enantiomer shows more potency and more affinity to the 5HT_{2A} receptor than S-enantiomer [5]. In drug discrimination studies in LSD-trained rats, used as an initial screen for evaluating the behavioural activity or hallucinogenic potential of new molecules, BDF was slightly more potent than LSD [5,19]. Furthermore, BDF showed to be a very potent ligand for the cloned human 5HT_{2A} and 5HT_{2C} receptors [19]. BDF also acts at 5HT_{2B} receptor, but with an affinity lower than at 5HT_{2A} receptor [21]. In addition, some data suggest that BDF acts as an agonist at α ₁-adrenergic receptor [4,22]. The action at both α ₁-adrenergic receptor and serotonin receptor in blood vessels could explain BDF induced severe vasoconstriction [4,22].

Modalities of consumption

Like LSD, BDF is generally used in the form of impregnated paper. Some reports suggest the use of BDF via nasal insufflation and liquid administration, occasionally in tablets. Liquid formulation is sometimes assumed onto sugar cubes. Finally, intravenous administration has also been reported [4,7,10,12]. Users information suggests that BDF is often taken in combination with other psychotropic substances such as: amphetamines, cocaine, synthetic cathinones, ketamine, cannabis, alcohol, benzodiazepines, kratom, LSD, 2C-B [4,7,10].

Toxicology

BDF is used by people for its long lasting LSD-like effects [4]. Dose range reported is between 100-2100 μ g, in particular, the more potent European batch is generally active at 200- 500 μ g while the less potent American batch” is active at 800-2100 μ g [12,23]. Desired effects include: kaleidoscopic hallucinations, altered perception of space and time, high resolution colourful visuals, shimmering lights, increased energy, increased associative thinking, well-being, prolonged sexual pleasure, and mild euphoria. Users reports suggest onset of psychotropic effects within 20-90 minutes of oral ingestion and within 30-60 minutes of nasal insufflation [4,7,10]. Users also reported delayed onset of action for up to 6 hours after oral ingestion, in particular if BDF is taken on a full stomach. In this circumstance, the users can assume another dose or another drug thinking that the first dose was insufficient to cause any psychotropic effects [4,7,10]. The duration of action is between 6-24 hours with a prolonged come down phase up to 2-3 days [4,7,10]. Undesirable effects include: prolonged hallucinations and euphoria, flashback, anxiety, severe insomnia, headache, nausea, diarrhoea, sweating, tightness, twitches, muscle tension, confusion, memory alterations, delusions and paranoid ideation [4,7,10]. In the reported cases that required medical care after recreational consumption of BDF, the most common side effects were: tachycardia, blood hypertension,, hyperpyrexia, mydriasis, psychomotor agitation, hallucinations, generalised seizures, rhabdomyolysis, respiratory problems, liver and kidney failure, and peripheral ischaemia [24-27]. Patients were treated with a variety of vaso-dilating drugs such as ACE inhibitors, nitroprusside, prostacyclin analogs, glyceryl tri-nitrate, calcium channel blockers, but none of them was reported to be effective [26,27]. Kidney failure was treated with veno-venous hemodiafiltration while complications such as aspiration pneumonia and respiratory problems were treated with intravenous antibiotics and respiratory assistance [25-27]. When were present, agitation and psychotic symptoms were treated with large doses of intravenous benzodiazepines [24,25].

Fatalities

Some deaths related with the consumption of BDF have been signalled in different countries such as Sweden, Norway, Finland, Denmark and USA [3,6,7,26-28]. However, very little information have been published about the post-mortem toxicological analysis. In the case reported in Denmark, a 18-year-old woman was found dead after consumption of BDF in liquid form. BDF was detected in femoral blood at the concentration of $4.7 \pm 0.7 \mu\text{g/kg}$ (double determination in two analytical series). The concentration of BDF detected in urine and vitreous humour were $22 \pm 2 \mu\text{g/kg}$ and $0.5 \pm 0.1 \mu\text{g/kg}$, respectively. The autopsy findings revealed oedema of the lungs, slight oedema of the brain, enlargement of the spleen, irritation of the mucous membranes in the stomach and ischemic changes in the kidney. Blood concentration of BDF found in the deceased woman was 8 times higher than those found in the samples of two men hospitalized after recreational use of BDF [3].

Medical use

To date, there are no approved indications for BDF in human pharmacology, however, it is known the involvement of 5HT receptors in the regulation of intraocular pressure in humans. Some studies have shown that various serotonin 5HT_{1A} and 5HT_{2A} receptor ligands, including BDF and several of its analogs, cause intraocular hypotensive activity in monkeys and rabbits after topical application [28,29]. It has been hypothesized that serotonin 5HT receptor agonists without psychotropic effects could be developed for the treatment of ocular hypertension and glaucoma in humans [29].

Discussion

Hallucinogenic substances have been used by indigenous cultures for millennia, however, the use was generally restricted to sacramental and healing contexts and regulated by ceremonial guidelines [30-32]. In the last decades, these substances have received large popularity among young drug users who experience their effects principally in “rave or party scenes” [33-35]. Recreational use of hallucinogens has favoured the spread of increasingly more powerful and legal molecules capable of satisfying the needs of the users [35]. In particular, the use of internet as a potential source of information on drugs of abuse [36] resulted in the use of several research chemicals as recreational drugs in place of traditional and illicit substances [1,37-42]. BDF is a research chemical synthesized in 1998 to investigate CNS serotonin receptor structure and activity [5]. This molecule is a very potent and long-acting agonist at 5-HT_{2A} receptor used by people for its LSD-like effects [4,18,35]. In fact, as showed from several evidence, 5HT_{2A} receptor is the main site for hallucinogen action and the entire most common hallucinogenic drugs act as agonist on this receptor [43]. It is considered the first aryethylamine derivative to surpass LSD in potency in a behavioural assay and the first molecule with LSD-like activity to have an aromatic nucleus other than benzene or indole [19]. This molecule appears to be typically sold by online research chemicals suppliers because the synthesis is complicated for the usual clandestine chemist and requires sophisticated instrumentations [44]. Pattern of acute toxicity emerged by both the cases of intoxication signalled in some countries and the users reports present within the drugs forum include psychedelic effects combined with an amphetamine-like activation [4,7,10,25,27-29]. Furthermore, the capability of over stimulating the 5HT_{2A} and α ₁-adrenergic receptor could explain the contraction of vessels smooth muscle cells and consequently the severe vasoconstriction [4,23,44]. BDF is considered a substance that causes concern in terms of its potency and toxicity and many countries have published warnings

alert about its toxicity [9,44] Vulnerable people could be encouraged to use BDF by online comments and videos emphasizing its powerful and the long lasting hallucinogenic activity [35]. Furthermore, in so called “rave or party scene”, some users could unknowingly assume this hallucinogen because sold in substitution of LSD [4,18]. Considering the high clinical toxicity, the alertness of medical community is of great importance in order to track and monitoring the spread of this powerful serotonergic hallucinogen.

Conclusion

BDF is a potent and long-acting psychedelic drug producing both LSD-like effects and amphetamine activation. Information currently available suggests that this drug can produce severe intoxications with serious medical complications including rhabdomyolysis, respiratory problems, liver and kidney failure, peripheral ischaemia and psychosis. Pharmacological potency and clinical toxicity associated with the consumption of this substance are reason of concern within the medical community. A better international cooperation is indispensable in order to monitoring and preventing the spread of this dangerous recreational substance.

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