Designer benzodiazepines gidazepam and desalkygidazepam (bromonordiazepam): What do we know?

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Abstract

Designer benzodiazepines are one of the primary new psychoactive substances (NPS) threats around the world, being found in large numbers in post-mortem, driving under the influence of drugs (DUID) and drug facilitated sexual assault (DFSA) cases. Even though when compared to many other NPS types, such as opioids and cathinones, there are relatively few designer benzodiazepines being monitored. Recently a new NPS benzodiazepine has been reported in Europe, the USA and Canada, desalkygidazepam, also known as bromonordiazepam. This substance is a metabolite of the pro-drug gidazepam, a drug licenced for use in Ukraine and Russia under the name Gidazepam IC\textsuperscript{®}. In the paper we review what is currently known about the use, pharmacology and analytical detection of gidazepam, its metabolite desalkygidazepam, and their other possible metabolites.

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Introduction

Designer benzodiazepines, more correctly termed new psychoactive substance (NPS) benzodiazepines, are one of the primary NPS threats around the world being found in a large number in post-mortem, driving under the influence of drugs (DUID) and drug facilitated sexual assault (DFSA) cases (1, 2). In Europe the first report of an NPS benzodiazepine to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) was the emergence of phenazepam in 2007 (1). As of October 2022, the EMCDDA are monitoring 35 NPS benzodiazepines. Most of the NPS benzodiazepines that are being monitored are orphan drugs that were patented by drug companies but then abandoned without being brought to the market (3). However, some of the NPS benzodiazepines are drugs that have been licenced for clinical use but are restricted to specific geographical areas/countries. The most common NPS benzodiazepine of this type being etizolam, licenced for use in Japan, Italy, and India, which has become one of the most abused NPS benzodiazepines around the world (2). The producers of NPS are always looking for new drugs to market, particularly ones that may avoid relevant drug legislation around the world. There are two benzodiazepines with limited geographical distribution, Cinazepam (Levana IV®) and Gidazepam (Gidazepam IC®) that are prescription only medicines in Ukraine and Russia respectively and that had not emerged as NPS benzodiazepines until recently. Cinazepam was first reported to the EMCDDA in 2019, and while gidazepam has not currently emerged as an NPS benzodiazepine, there are concerns that it may soon (4, 5). The active metabolite of gidazepam, desalkylgidazepam, has recently been reported to the EMCDDA and has also been detected by drug testing services in Canada (6), the UK (7) and the USA (8). To date there is limited information about gidazepam and desalkylgidazepam outside of the Ukrainian and Russian language literature. In this paper we review what is currently known with regards to the use, pharmacology and analytical detection of gidazepam, desalkylgidazepam and their potential metabolites.
Gidazepam (CAS number 129186-29-4; 2-(7-bromo-2-oxo-5-phenyl-2,3-dihydro-1H-1,4-benzodiazepin-1-yl)acetohydrazide; Figure 1) also known as hydazepam or hidazepam is a 1,4-benzodiazepine that was developed in Kyiv, Ukraine in the early 1990s. Gidazepam is available as a prescription only medicine under the trade name Gidazepam IC® in Ukraine and Russia, being released to the market in 1997 (9), in both tablet and sublingual formulations (10). In 2016 gidazepam had around 7.7% of the market share of anxiolytic market in Ukraine (11). As with many other benzodiazepines gidazepam is used to treat anxiety, alcoholic withdrawal, migraines and is also used pre-operatively, but it is not licenced for use in children (12). Gidazepam is available as either 20 mg or 50 mg tablets. The recommended dosage depends on the condition that is being treated and is 40-60 mg per day for migraines, 60-200 mg per day for anxiety associated disorders, and 50-500 mg per day for alcoholic withdrawal (12). The maximum recommended duration of use is 4 months (12).

Pharmacology of Gidazepam and its Metabolites

Pharmacokinetics

In the literature there are 2 human studies investigating the pharmacokinetics of gidazepam after oral dosing. The first study consisted of 5 individuals who were all administered 50 mg of gidazepam with blood samples being taken at sufficient intervals to allow the determination of various important pharmacokinetic parameters (see Table 1) (13). The second study was carried out on 18 individuals of between 20 and 50 years old. These individuals were given an initial gidazepam dose of 50 mg followed by a daily dose of 100-200 mg for up to 3 weeks (14). The only detectable substance in humans was the metabolite of gidazepam, desalkylgidazepam (see Figure 1). Desalkylgidazepam is also known as bromonordiazepam, due to the substitution of the chlorine atom in nordiazepam with a
bromine atom giving desalkygidazepam. The pharmacokinetic parameters determined from these studies are detailed in Table 1 and refer to desalkygidazepam. The volume of distribution (V_d) of desalkygidazepam is on average 4.27 L/kg, which is relatively high when compared to other benzodiazepines (3, 15). This high V_d indicates that in postmortem cases desalkygidazepam is likely to exhibit postmortem redistribution (16). The half-life of desalkylgidazepam is on average 86.73 h, this is longer than most benzodiazepines and would put gidazepam into the category of a long-acting benzodiazepine, as its half-life (t_1/2) is >24h (15). There are no in vivo studies in the literature on the bioavailability of gidazepam in humans but based on animal studies and other benzodiazepines it is likely to be >70% (17), with in silico studies putting the bioavailability at ~99% (18). Gidazepam is thought to be more rapidly absorbed into the blood from the gastrointestinal tract than other benzodiazepines (19). Desalkylgidazepam is thought to have a slower rate of absorption than its parent compound, but still within the typical absorption rates observed for other benzodiazepines (19).

Metabolism of gidazepam

As briefly mentioned above human studies have shown that gidazepam is a pro-drug that is quickly metabolised via dealkylation into its active metabolite desalkylgidazepam, although other metabolites have been described (see Figure 1). To date only desalkylgidazepam has been detected in blood following the administration of oral gidazepam (13, 14). It is however possible that with newer analytical techniques with increased sensitivity (such as LC-MS/MS or LC-TOF-MS), that these metabolites may be found to be present in low concentrations in human blood. All the metabolites of gidazepam shown in Figure 1 have been detected in urine in the following approximate percentages (gidazepam 6-15%; desalkylgidazepam 10-15%; carboxymethylgidazepam (50-70%) and 3-hydroxydesalkylgidazepam glucuronide (5-15%). No data has been given in the literature about the likely concentrations of these
metabolite that have been seen in urine analysis (20). The only study carried out to investigate the metabolic enzymes involved in the phase I metabolism of gidazepam in humans is an in silico one that suggests that CYP2D6 and CYP3A4 are the major metabolic enzymes involved (18). There are, however, mice studies that show CYP2C19 is involved in the metabolism of gidazepam, at least in animals (21). These enzymes are commonly involved in the metabolism of other benzodiazepines (3). The only phase II metabolite that has been reported in the literature is the glucuronide of 3-hydroxydesalkylgidazepam (20), it is unclear which metabolic enzyme is involved.

Pharmacodynamics

In vitro and in silico studies

As with other 1,4-benzodiazepines, gidazepam and its metabolites bind to, and have activity via, the gamma-aminobutyric acid type A (GABA-A) receptor (see Table 2). Gidazepam also binds to the translocator protein (TSPO), (22) (formerly known as the peripheral benzodiazepine receptor (23)), with gidazepam being shown to have a 3-fold higher affinity for the translocator protein than CNS benzodiazepine receptors (IC$_{50}$ 710 nmol/L and 2200 nmol/L respectively (22)). Another NPS benzodiazepine, 4'-chlorodiazepam (reported to the EMCDDA in 2016), also binds strongly to the translocator protein (24). However, 4’-chlorodiazepam does not bind to the GABA-A receptor, in contrast to gidazepam. The pharmacological actions elicited by the binding of benzodiazepines to the translocator protein are as yet, unclear but may involve stimulating the synthesis of neuroactive steroids such as allopregnanolone. These neuroactive steroids are positive allosteric modulators of GABA-A receptors and produce similar physiological effects to benzodiazepines upon binding to these receptors (25). The interaction of gidazepam and its metabolites to the GABA-A receptor have been characterised by both in vitro displacement binding studies (26, 27) and in silico
studies (28). Gidazepam has been described as a partial agonist of the GABA-A receptor (27). The Ki of gidazepam is 2200 ± 50 nM and the Ki of desalkylgidazepam is 3.5 ± 0.2 nM, suggesting that desalkylgidazepam has the greater affinity for the GABA-A receptor (27). The metabolite carboxymethylgidazepam is considered to be inactive. The pharmacological potencies of gidazepam and its metabolites are mirrored by *in vivo* models of seizure activity that use pentylenetetrazol (corazole) to induce seizures. These results again show that carboxymethylgidazepam is inactive with desalkygidazepam being the most potent of the remaining parent drug and metabolites (29) (see Table 2).

**Clinical and in vivo studies**

In clinical and other *in vivo* animal studies gidazepam has been shown to have a unique spectrum of pharmacological activity that distinguishes it from other benzodiazepines. Gidazepam has prominent anxiolytic properties without producing the sedative and muscle relaxant effects that are associated with other benzodiazepines, such as diazepam (22). This has been demonstrated in both animal models and clinical (human) studies. A study into the pharmacological effects of gidazepam and diazepam on inbred C57BI/6 (B6) and Balb/c (C) mice using ‘open-field’ testing, found that diazepam at low doses either stimulated the behaviour of C mice or inhibited the activity of B6 mice. In comparison, gidazepam had a low dose range which activated the behaviour of C mice, without having a sedative effect on B6 mice (30). This suggests a wide separation between the anxiolytic and sedative dosages of gidazepam, when compared with diazepam, an example of a typical benzodiazepine.

In human studies the lack of sedative effects of gidazepam is confirmed as when given in a controlled study where subjects were either given 100 mg gidazepam or a placebo for 14 days and asked to perform psychological testing investigating alertness, reaction time, attention and memory there was no significant difference between the placebo and gidazepam (31, 32).
“Trip reports” from illicit use of desalkylg idazepam (bromonordiazepam)

Reports from the internet of illicit use (so called “trip reports”) can be beneficial in understanding the effects of new NPS drugs (33, 34) It is however important to note that the users and posters of these reports firstly do not know if the drug they are taking is what they think they are taking and secondly it may not be the only drug they are taking at that time (33, 34). Searches on the internet by the authors have shown that desalkylg idazepam is being advertised for sale on numerous “research chemical” websites for sale either as a powder or as 1 mg or 2.5 mg “pellets” or 3 mg tablets. These research chemical websites are quoting a dose of 6-9 mg for desalkylg idazepam and this dosage is supported by the various trip reports. The trip report comments also confirm the lack of sedative effects, the long half-life, the anxiolytic effects, but also that gidazepam and desalkylgidazepam use may not become widespread. Some comments are: “It's a quite functional benzo, very little hypnotic effects but eliminates anxiety very well [...] I've got up to 30 mg with it and no ill effects from that dosage [...] I feel like it would be a good tapering benzo due to the long half-life and not much recreational potential (35). “I tried bromonordiazepam and it was the worst I've ever tried [...] the effects were weird. It made me unable to think clearly, it felt like I've only got two brain cells left. [...]. I had a breakdown taking this after staying awake for three days and it totally escalated. I ended up in the hospital after having a fight with my boyfriend about literally nothing. I was acting totally crazy. Absolutely not recommended! (35) and “I did 9 mg one hour after breakfast [...] It felt like 15 mg of diazepam would feel, but with less sedation and with next to no muscle relaxation. [...] highly specific for anxiety reduction, 9 mg had no mellow feeling you'd get from diazepam”. [bromonordiazepam] worked very subtle, that's probably the reason why folks with tolerance get next to nothing out of it, but I'm sure it could be a good option for a taper. [...] [I] couldn't see any real

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1 For ethical reasons no information for specific sites are given.
recreational advantage of the drug.” (36) “Well it [...] feels like diazepam except it works for almost two days.” (37) “with no benzo tolerance I found 6 mg being a good anti-anxiety drug. I haven’t pushed it higher than 9 mg, but it had obvious benzo type effects from 9 mg” “Desalkylgidazepam [effects are] mostly anti-anxiety, not super heavy sedation. I did feel good though…. might be ok for maintaining” (38). Overall, the trip reports suggest that it is not really a recreational drug, does not show sedating properties, but does show good anxiolytic effects. The trip reports do not mention many side effects, beyond those normally expected of benzodiazepines.

Gidazepam and metabolites blood concentrations and side effects

Blood Concentrations of gidazepam and its metabolites

The human studies with oral gidazepam dosing allow us to understand the blood concentrations of desalkylgidazepam that will likely be found with clinical usage. When a blood sample was taken 4 hours after an initial 50 mg dose of gidazepam, a mean desalkylgidazepam concentration of 0.19 mg/L (range 0.06-0.48 mg/L; median 0.15 mg/L) was observed (14). In this study the initial dose of gidazepam was followed by a gidazepam dose of 100-200 mg (mean 129 mg) for up to 3 weeks to mimic clinical usage (14). 14 days after the initial 50 mg dose was given a blood sample was taken allowing the determination of the desalkylgidazepam concentration at steady state. The mean desalkylgidazepam concentration at steady state ($C_{ss}$) was 2.68 mg/L (range 0.93-6.00 mg/L; median 1.73 mg/L), no further pharmacodynamic information was presented in the study after day 14 (14). When a single 50 mg dose of gidazepam was given to 5 individual the average peak blood gidazepam concentration observed was 0.103 mg/L (13). To date there have been no
published studies on the concentrations of gidazepam or any of its metabolites in overdose, from post-mortem or driving under the influence cases.

*Side effects of gidazepam and its metabolites*

Although gidazepam has demonstrated relatively mild and few side-effects, in comparison to other benzodiazepines during clinical use at therapeutic level doses, it still holds the potential to cause significantly more serious and harmful effects at higher dosage levels. Reported side effects from clinical use include, drowsiness, weakness, myasthenia gravis, addiction, dysmenorrhea and allergic reactions (39). Recreational use of gidazepam, like other benzodiazepines, poses a significantly higher risk of negative effects, particularly if used in combination with other substances (40). Large doses of gidazepam, especially in the elderly, are reported to cause impaired coordination, ataxia, as well as severe muscle weakness. These effects are noted to reduce 1-2 days after dose reduction or complete withdrawal (41). Known effects from interactions with other substances include the enhancement of the effects from alcohol, hypnotics, neuroleptics, antipsychotic drugs and narcotic analgesics (42).

*LD$_{50}$ of gidazepam and its metabolites*

Although there is limited information on gidazepam in overdose there is some information on its potential toxicity. The LD$_{50}$ (the amount of material given all at once, which causes the death of 50% of a group of test animals) from animals is not directly comparable with human toxicity but can give an indication of the potential comparative toxicity of a compound when compared to other similar compounds. As the LD$_{50}$ of gidazepam and its metabolites has been determined in mice (29) we can compare them to the LD$_{50}$ of etizolam and diazepam (43). As can be seen from Table 3 the toxicity in order of potency is desalkygidazepam>diazepam>3-hydroxydesalkylgidazepam>gidazepam>etizolam>carboxymethylgidazepam. These data suggest that gidazepam has a similar comparative toxicity to etizolam and its main metabolite
desalkylgidazepam has a similar toxicity to diazepam. It is important to note that benzodiazepines are considered to have a very good safety profile when using clinically (44).

Analysis of gidazepam and its metabolites

The analysis of gidazepam and its metabolites, particularly desalkylgidazepam, is important for understanding their use, abuse and potential risks of use. To date several methods have been described in the literature for both the extraction and analysis of gidazepam and its metabolites.

Extraction

Studies have shown that gidazepam and its metabolites can be extracted from blood, tissues and urine using both solid phase extraction (SPE) and liquid-liquid extraction (LLE) with high extraction efficiency.

Solid phase extraction (SPE)

For SPE the extraction efficiency was, on average, between 72% and 98% for gidazepam and its metabolites (desalkylgidazepam, carboxymethylgidazem and 3-hydroxydesalkylgidazepam) in blood and urine (45), when using a 3 ml Agilent Bond Elut Certify SPE column and a slightly adapted version of the methodology given in (46). The SPE column was conditioned with 2 ml of methanol, 2 ml of distilled water and 1 ml of 0.1 M phosphate buffer solution (pH 6.0). Following the conditioning 1 ml of sample (1 ml of either blood or urine) was loaded into the column. The column was then washed with 3 ml of distilled water, 1 ml of 1 M acetic acid, 3 ml of methanol and then air-dried for 5 min. The analytes were eluted from the column with a 2 ml of a mixture of dichloromethane/IPA/ammonia solution (78/20/2). The eluate was then evaporated to dryness at ≤ 40°C. The eluent can then either be reconstituted in mobile phase for HPLC use or derivatised with 50 µL of BSTFA (with 1% TMCS) for 20 minutes at 70 °C.
Liquid-liquid extraction (LLE)

The earliest published methods of analysis of gidazepam and its metabolites utilised double ether extraction at pH 9.0 (14, 47) with an average extraction efficiency for gidazepam of 76%, desalkygidazepam of 80% and 3-hydroxydesalkylgidazepam of 83% (14). The use of ether was a common extraction method for benzodiazepines in the past (48) but due to modern health and safety concerns it has been replaced by safer solvents. A more recent study investigated the use of various solvents for the extraction of desalkygidazepam. The two most efficient solvents are ethyl acetate (98%) and a chlorobutane:ethyl acetate mix (9:1). The method of extraction is as follows: to 1 ml of blood, 1 ml of borate buffer solution (pH 9) was added. This was followed by 5 ml of chlorobutane:ethyl acetate or ethyl acetate. After 5 minutes of the sample was centrifuged for 5 minutes at 3000 rpm. The organic phase was removed and evaporated under air at 40 °C (20). This was followed either by reconstitution in mobile phase or derivatisation (see below), depending on the analytical method to be used.

Chromatographic analysis of gidazepam and metabolites

Methods Using HPLC-UV and GC-GC-MS methods have been published for the detection of gidazepam and its metabolites. The published methods are described in detail below.

GC-GC-MS Analysis

Blood and Tissues

The Two-Dimensional Gas Chromatography mass spectrometry (GC-GC-MS) methodology for the detection and quantitation of gidazepam and metabolites is described in detail in (49, 50). The method was validated according to UN guidelines (51). In brief, an Agilent
6890N/5973N/FID GC-MS fitted with a Deans switch (52) was utilised. The switch allows the carrier gas to be sent either via column 1 (HP5MS 0.25mm x 30m) to the FID detector or via Column 2 (DB17MS 0.25mm x30m) to the MS detector. The quantitation of desalkylgidazepam was validated for both tissue (exact tissue used not further described) (1 g) and blood (1 ml), with phenazepam (1µg/ml) being used as the internal standard. This was the extracted (as detailed above) and then derivatised with BSTFA. The method had an LOD of 3 ng/ml (blood) and 5 ng/g (tissue). The calibration range was 20-1000 ng/ml in blood and 0.2 – 10 µg/g in tissues. The \( r^2 \) of the calibration curve was 0.999 assuming a linear model, with inter and intraday precision of the method being <15%.

Urine

This method describes the detection of benzodiazepine benzophenones following alkaline hydrolysis of urine. The advantage of this method is that the benzophenone aminocarboxy bromobenzophenone (ACBB; Figure 2) is unique to gidazepam allowing the confirmation of gidazepam use. The alkaline hydrolysis was carried out as follows: To 1 mL urine in a screw-capped test-tube 0.15 mL of 40% (w/w) sodium hydroxide was added, the cap was screwed on to the test-tube and it was allowed to stand in a boiling water-bath for 20 min. After hydrolysis, the test-tube was cooled, and the pH was adjusted to 2-3 for liquid-liquid extraction (LLE) or to pH 6-7 for solid-phase extraction (SPE) with 2.0M hydrochloric acid.

HPLC Analysis

Method 1 (13): A HPLC-UV method for the quantitation of gidazepam and its metabolites (I-IV). This method used a Beckman Altex 160 Absorption Analyzer HPLC System. The flow rate was 1 ml/min and used an ethanol: glycine buffer (pH 2.2) mobile phase (4.3:5.7). This isocratic method used an Ultrasphere C-18 (5 µm, 4.6 x 150 mm) column at room temperature. The UV detection was set to 254 nm. Diazepam was used as the internal
standard. Gidazepam and metabolites were extracted from blood plasma by double extraction with diethyl ether at pH 9.0. No information was provided about the validation, LOD, LOQ, or the concentrations of the analytes used in the calibration curve.

**Method 2** (53): A HPLC-UV method for the quantitation of gidazepam and its metabolites (I-IV) The method used a Perkin Elmer HPLC equipped with an isocratic pump (PE-250) and UV detector (PE-290). The flow rate was 1.5 ml/min and used an 0.02 M MOPS (3-(N-morpholino)propanesulfonic acid):1N HCl :acetonitrile:methanol (40:1:22.5:2.5) buffer. This isocratic method used a LiChrosorb® RP-18 (7 µm, 4.6 x 250 mm) column at room temperature. The injection volume was 20 µl. The UV detection was set to 232 nm. Experimental samples (obtained by centrifugation of blood at 3000 rpm for 15 min) were added with a two-fold volume of 1 M borate buffer (pH 9.0) and extracted with a 10 x volume of diethyl ether for 10 min on an electric shaker. The extraction was carried out twice. For the subsequent purification of the analysed compounds, acid back extraction with a 6 M hydrochloric acid solution followed by neutralization with a 6 M sodium hydroxide solution was used. The neutralized solution was shaken twice with an equal volume of freshly distilled ether. The ether extracts were purified and evaporated in a stream of nitrogen, after which the test tubes were placed in a vacuum desiccator with phosphorus pentoxide for 2 hours. The dry residue was dissolved in 0.1–0.3 ml of acetonitrile containing an external standard (diazepam, 8 µg/ml): The calibration curves were described as being linear between 0.5-10 µg/ml (number of points unknown) with an R² of >0.999. The retention times were as follows: - gidazepam 3.68 min, desalkygidazepam 5.29 min, diazepam 8.0 min. The LOD was 45.0 ng/ml and for desalkylgidazepam - 40.0 ng/ml. The percentage of extraction of gidazepam was on average 76 % and for desalkylgidazepam was 80 %.
It is expected that up-to-date methods of benzodiazepine analysis as detailed in (3) would be easily adapted for the detection and quantitation of gidazepam and metabolites if LC-MS/MS analysis was required.

**Conclusions**

Gidazepam and its active metabolite desalkygidazepam are benzodiazepines that may soon become drugs of abuse. This paper allows forensic and clinical practitioners to understand what is known about gidazepam and its metabolites to date and how to analyse them should they become commonly used and abused.

**Data availability statement**

There are no new data associated with this article.

**References**


**Table 1:** Pharmacokinetic properties of desalkylgidazepam in humans following a 50 mg dose (n = 5). All data taken from (13).

<table>
<thead>
<tr>
<th>Pharmacokinetic Parameter</th>
<th>Value</th>
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<tr>
<td>C&lt;sub&gt;max&lt;/sub&gt;</td>
<td>0.103 ± 0.018 mg/L</td>
</tr>
<tr>
<td>T&lt;sub&gt;max&lt;/sub&gt;</td>
<td>4.8 ± 2.3 h</td>
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<tr>
<td>Plasma clearance (Cl&lt;sub&gt;app&lt;/sub&gt;)</td>
<td>0.035 ± 0.002 L/h/kg</td>
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<tr>
<td>Volume of distribution (V)</td>
<td>4.27 ± 0.91 L/kg</td>
</tr>
<tr>
<td>Substance</td>
<td>( \text{in vitro} \text{ Ki} ) (mol/L)</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>------------------------------------------</td>
</tr>
<tr>
<td>Gidazepam</td>
<td>(2200 \pm 76)</td>
</tr>
<tr>
<td>Desalkygidazepam</td>
<td>(12.0 \pm 0.2)</td>
</tr>
<tr>
<td>Carboxymethylgidazepam</td>
<td>(&gt;2000)</td>
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<tr>
<td>3-hydroxydesalkylgidazepam</td>
<td>(14.5 \pm 0.6)</td>
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Table 2: Pharmacodynamic parameters for gidazepam and its metabolites. All data taken from (26, 29).
Table 3: Acute oral LD$_{50}$ values of various benzodiazepines in mice.

<table>
<thead>
<tr>
<th>Benzodiazepine</th>
<th>LD$_{50}$ (mg/kg)</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Desalkygidazepam</td>
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<td>(29)</td>
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<td>Diazepam</td>
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<td>(43)</td>
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<tr>
<td>3-hydroxydesalkylgidazepam</td>
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<td>(29)</td>
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<tr>
<td>Gidazepam</td>
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<td>(29)</td>
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<td>Etizolam</td>
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<td>(43)</td>
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<tr>
<td>Carboxymethylgidazepam</td>
<td>&gt;2000</td>
<td>(29)</td>
</tr>
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</table>

Figure 1: Metabolism of Gidazepam: I – Gidazepam, II – Carboxymethylgidazepam, III – Desalkylgidazepam (bromonordiazepam), IV 3-hydroxydesalkylgidazepam
Figure 2: Formation of gidazepam metabolite aminobenzophenones by hydrolysis. II – Carboxymethylgidazepam, III – Desalkylgidazepam (bromonordiazepam), IV 3-hydroxydesalkylgidazepam, V - aminocarboxybromobenzophenone (ACBB) VI - aminobromobenzophenone (ABB)