

Comparative Study of Solubility of Tranquilizers (Alternative Date Rape Drugs) in Stomach Acid

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Abstract: Date Rape Drugs are the members of tranquilizers and sedative class of drugs. These are the substances that make it easier for someone to rape or assault sexually. The person who is administrated by these drugs can cause sleepiness, slow breathing, slow heartbeat rate, trouble in muscle coordination, loss of consciousness. GHB (gamma-hydroxybutyric acid), Rohypnol (flunitrazepam), Ketamine are generally considered as date rape drugs. As Food and Drug Administration Department of Central Government of India considered this issue and placed these drugs under the schedule of Narcotic Drugs and Psychotropic Substances Act. Thereafter it is nearly impossible to get these drugs easily. But criminals have been searched new way through it. Normal tranquilizers and sedatives are also being used for committing such crimes. These drugs are also scheduled, but one can get them with prescription from a registered medical practitioner. So we carried out a comparative study of 3 tranquilizers from the benzodiazepine class that are Diazepam, Alprazolam, and Librium to check their dissolving rate in stomach acid. Estimation of action time of drug can help an investigator to identify the class of drug and time of drug injected (early phase). In our study, we found that the dissolving period of Diazepam and Alprazolam is more than conventional drugs.

Key words: GHB (gamma-hydroxybutyric acid), Rohypnol (Flunitrazepam), Ketamine, Narcotic Drugs, Psychotropic Substances Act.

1. Introduction

Date rape drugs are drugs used to assist in a sexual assault, which is any type of sexual activity a person does not agree to. Drugs or alcohol can make person confused about what is happening with him/her, unable to defend themselves against the ongoing sexual assault, or unable to remember what happened. Generally the term 'Date Rape Drug' is used, but the person who commits such crime may not be in relationship or on date [1]. Accused might be friend, neighbor or any known/unknown person. In India, Rape is fourth most common crime against women in India. According to NCRB (National Crime Record Bureau) in 2019, 32,033 rape cases were registered across the country (Figure 1).

The Date Rape drugs are most commonly used in metropolitan area. Use of these drugs is common in

high profile celebrations, parties, night clubs etc. Hence these drugs are also known as club drugs. These date rape drugs generally include flunitrazepam (Rohypnol), gamma-hydroxybutyric acid (GHB), gamma-butyrolactone (GBL), and ketamine [1-3]. These drugs also have their street name, so that they can be mentioned, transported easily for inappropriate intention.

Street names for GHB are Grievous Bodily Harm, Liquid G, Liquid Ecstasy, Somatomax, Cherry Meth, Easy Lay and Gamma10. Street names for ketamine are Special K, Ket and K, Vitamin K, Kit Kat, Keller, Cat Valium, Purple and Super C.

Street names for rohypnol are Roofies, R2, Roofenol, Roche, Roachies, La Rocha, Rope, Rib, Circles, Mexican Valium, Roach-2, Roopies, Ropies, Forget Pill, Trip-and-Fall and Mind Erasers. These drugs are from tranquilizer and sedative category, victim who is targeted by these drugs may feel dizzy, sleepy, calm, confused. After the activity of drug in blood, person may lose consciousness, unable to perceive things, resist wrong actions, control muscle co-ordination.

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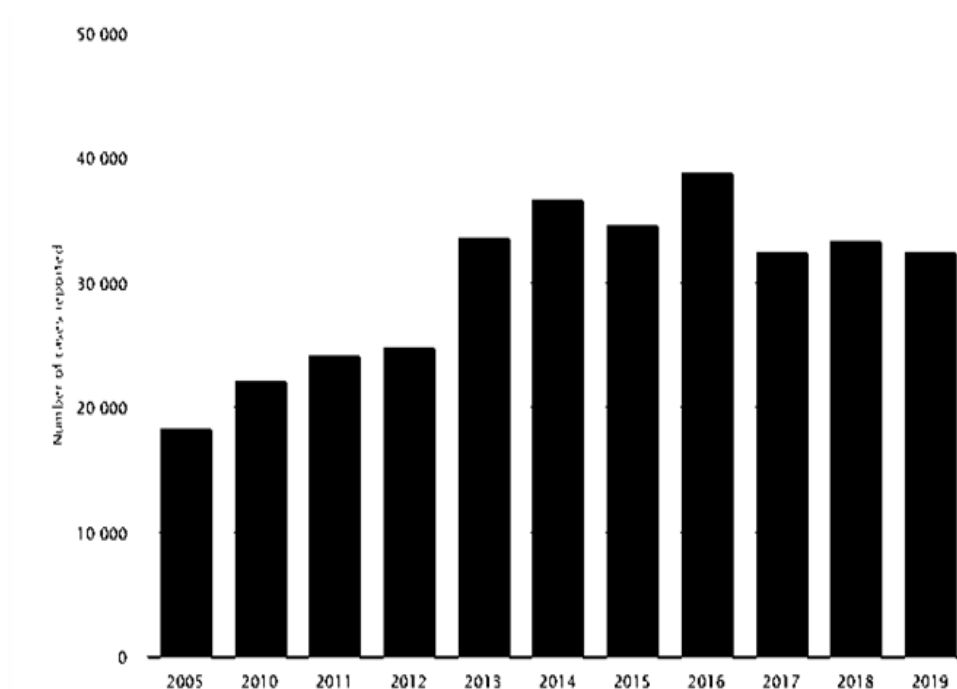


Fig. 1 Total number of rape cases reported in India from 2005 to 2019.

GHB [3]: It is usually a liquid that can be mixed with other liquid. It also comes in powder form. It has neither smell nor taste.

Rohypnol [4]: They are in form of white tablets that didn't have smell or taste. But drug manufacturer companies now make it as light green pills with blue dye.

Ketamine [8, 9]: It is clear liquid or off white coloured powder. It is also tasteless and odourless.

Looking into seriousness of increased crime rates, Food and Drug Administration department of Central Government of India banned Rohypnol and placed other drugs in schedule of Narcotics Drugs and Psychotropic Substances (NDPS) Act. In 2013, Ketamine was shifted from Schedule H to Schedule X of the Drugs and Cosmetics Rules to prevent its easy availability and misuse. As per the action taken by government, these Rohypnol, GHB, Ketamine are nearly impossible to get easily. But scenario is now changed. Due unavailability of these scheduled drugs, criminals have searched new path through it. Criminals are being moved to common tranquilizers and sedatives to commit crime. Tranquilizers from Benzodiazepine class are loosely

available in market [6]. One can get them with help of medical practitioner's prescription. This class includes drugs like Alprazolam, Chlordiazepoxide (librium), Clonazepam, Diazepam, Lorazepam, Midazolam, Oxazepam, Prazepam, flurazepam (Dalmene).

In this study, we have used 3 different drugs from benzodiazepine class to check the dissolved of drug and compare its rate of solubility.

1.1 Diazepam (Vallium)

Valium is a prescription medicine used to treat symptoms of anxiety, muscle spasm, alcohol withdrawal and as a sedative before surgery or to treat seizures. Valium may be used alone or with other medications [10, 11].

Valium (diazepam) is a benzodiazepine derivative. The chemical name of diazepam is 7-chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1,4-benzodiazepin-2-one. It is a colorless to light yellow crystalline compound. The empirical formula is $C_{16}H_{13}ClN_2O$ and the molecular weight is 284.75. Valium is available for oral administration as tablets containing 2 mg, 5 mg or 10 mg diazepam (Figure 2).

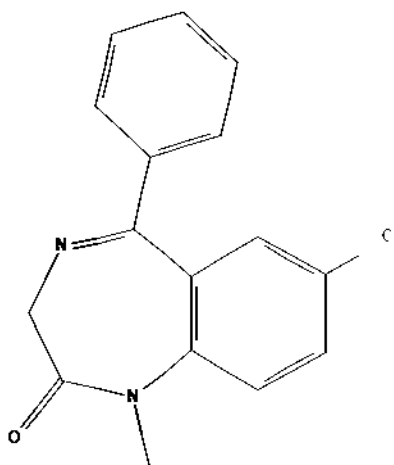


Fig. 2 Chemical Structure Depiction of Valium.

1.2 Alprazolam

Alprazolam is a prescription medication indicated for the treatment of anxiety disorder. Alprazolam tablets are also indicated for the treatment of panic disorder, with or without agoraphobia. This drug is also used as a treatment for anxiety associated with depression. This drug may be habit-forming and has the potential to cause extreme dependence or abuse in some patients. Side effects that are most commonly associated with this drug are drowsiness and light

headedness [12].

Alprazolam is available under the following different brand names: Xanax, Niravam, and Xanax XR. Drug is available in form of tablets for oral administration in 0.25 mg, 0.5 mg, 1 mg and 2 mg dosages. It's IUPAC name is 8-chloro-1-methyl-6-phenyl-4*H*-[1,2,4]triazolo[4,3a][1,4]benzodiazepine.

Formula of alprazolam is $C_{17}H_{13}ClN_4$ and molar mass is $308.77 \text{ g mol}^{-1}$ (Figure 3).

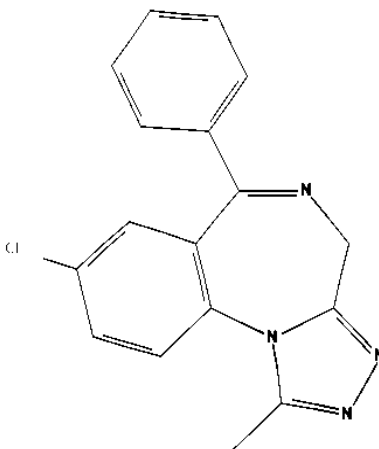


Fig. 3 Chemical Structure Depiction of Alprazolam.

1.3 Librium

Librium is a prescription medicine used to treat the symptoms of Anxiety. Librium may be used alone or with other medications [13].

Librium belongs to a class of drugs called Antianxiety Agents; Anxiolytics, Benzodiazepines. Chlordiazepoxide hydrochloride is 7-chloro-2-(methylamino)-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide hydrochloride. A white to practically white

crystalline substance, it is soluble in water. It is unstable in solution and the powder must be protected from light. The molecular weight is 336.22.

Librium (chlordiazepoxide) is available as capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl (Figure 4).

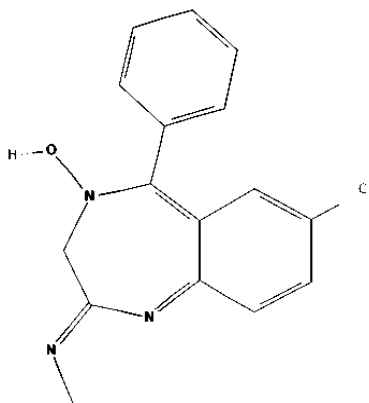


Fig. 4 Chemical Structure Depiction of Librium.

2. Materials and Methods

2.1 Materials

5 mg Diazepam manufactured by Abbott India

Pharmaceuticals Ltd (Figure 5A), 0.5 mg alprazolam manufactured by Torrent Pharma Ltd (Figure 5B) and 5 mg librium manufactured by Abbott India Pharmaceuticals Ltd (Figure 5C).

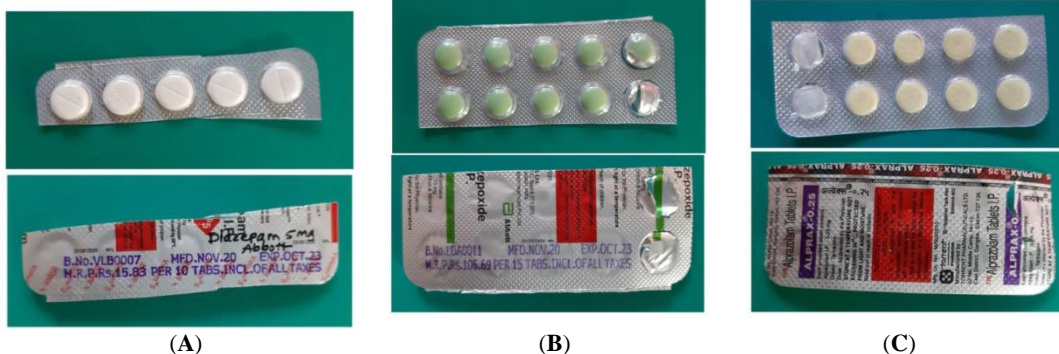


Fig. 5 (A): Diazepam 5 mg; (B): Librium 5 mg; (C): Alprazolam 0.5 mg.

2.2 Instruments

Conductivity Meter, Sonicator (Figure 6).



Fig. 6 Depiction of Sonicator cycles.

2.3 Chemicals

Figure 7 shows the conductance depictions of KCl

(Potassium Chloride), HCl (Hydrochloric Acid), NaCl (Sodium Chloride), and Stimulated Stomach Acid respectively.

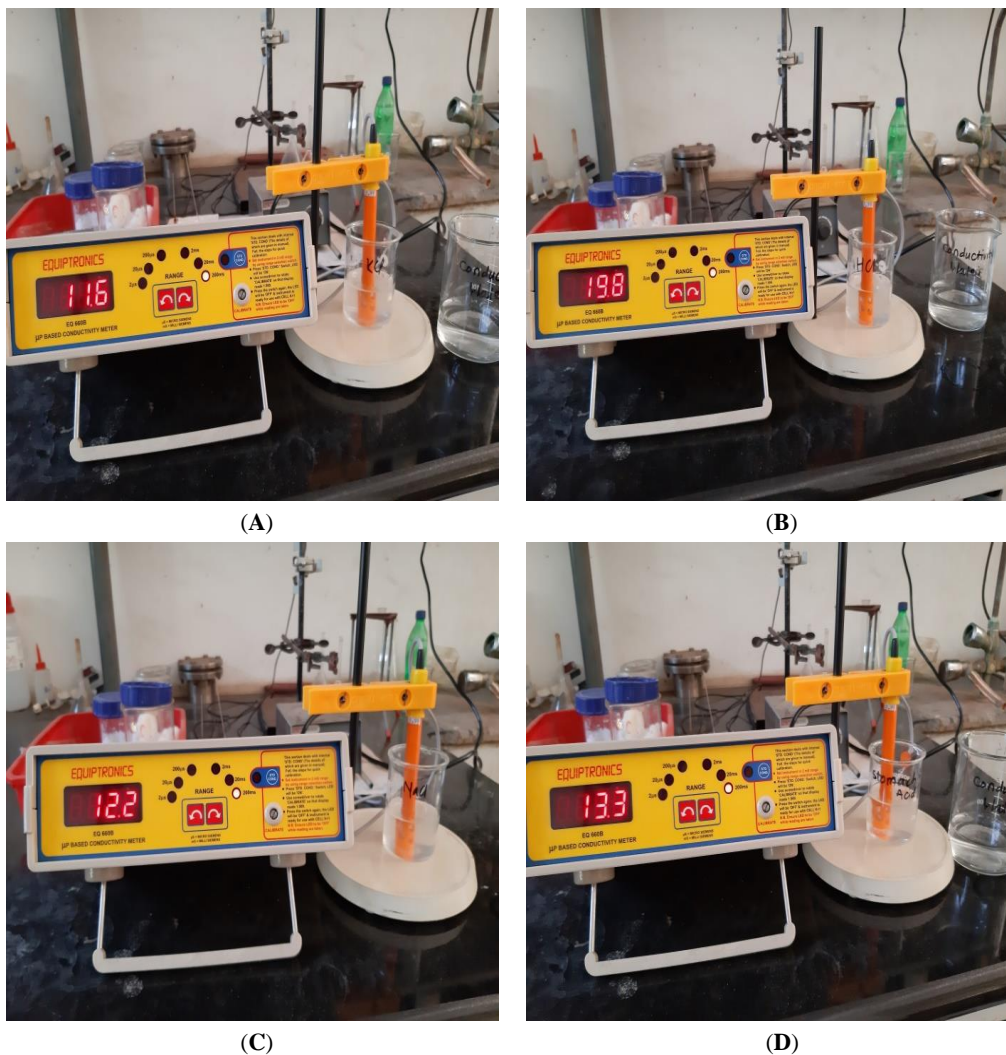


Fig. 7 (A): Conductance depiction of KCl (Potassium Chloride); (B): Conductance depiction of HCl (Hydrochloric Acid); (C): Conductance depiction of NaCl (Sodium Chloride), and (D): Conductance depiction of Stomach Acid.

2.4 Preparation of Stimulated Stomach Acid

For 1000 ml stimulated stomach acid, add 5 mg of Sodium Chloride in 1000 ml distilled water, mix well. Then add 5 mg KCL in solution. After to prepare 0.155 M HCl, add 5.6 ml of concentrated HCl in solution. Keep for 5 minutes. Solution is ready to use.

2.5 Preparing Solutions

Prepare 4 beakers A, B, C, D respectively.

Beaker A: Add 5 mg of NaCl in 1000 ml distilled water. Dissolve it. Take out 50 ml of solution in separate beaker, name it as A.

Beaker B: Add 5 mg of KCl in 1000 ml distilled water. Dissolve it. Take out 50 ml of solution in separate beaker, name it as B.

Beaker C: Add 5.6 ml of concentrated HCl in 1000 ml distilled water. Dissolve it. Take out 50 ml of solution in separate beaker, name it as C.

Beaker D: Take out 50 ml of Stimulated Stomach

Acid, name it as D.

2.6 Methodology

2.6.1 Checking conductance-Standardize conductivity meter

Adjust the knob on 200 m/s. Add 0.025 g (25 mg) drug sample in each beaker. Sonicate each beaker in Sonicator for 2 min maintaining temperature up to 37 to 40 °C. That is equal to the body temperature. Note down the conductance. Repeat the procedure for 15 cycles i.e. up to 30 min.

For each drug we carried out 15 cycles separately.

3. Results

3.1 Conductance Value of Diazepam, Alprazolam and Librium

For Diazepam, we carried out 15 cycles for NaCl, KCl, HCl and Stomach Acid. According to the readings, we plotted graph and found that conductance in NaCl is not changing significantly after 16 minutes. In KCl, conductance didn't change after 18 minutes. In HCl, conductance didn't change after 20 minutes. In Stomach Acid, conductance didn't change after 14 minutes (Chart 1).

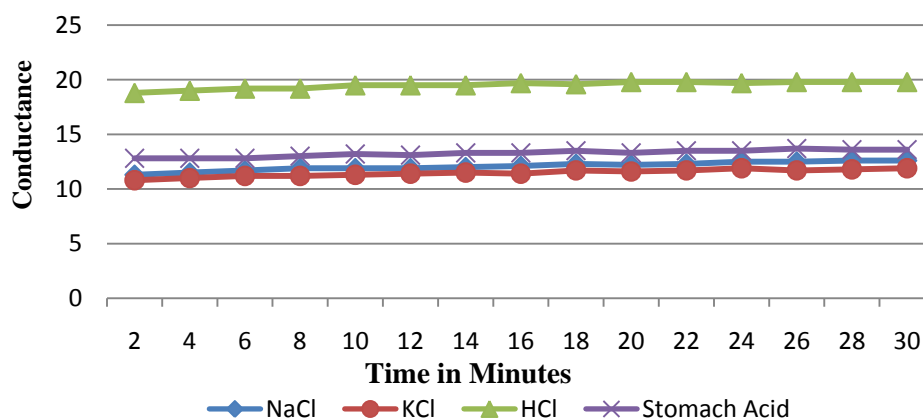


Chart 1 Conductance value of diazepam.

For Alprazolam, we carried out 15 cycles for NaCl, KCl, HCl and Stomach Acid. According to the readings, we plotted graph and found that conductance in NaCl is not changing significantly after 20 minutes.

In KCl, conductance didn't change after 12 minutes. In HCl, conductance didn't change after 12 minutes. In Stomach Acid, conductance didn't change after 12 minutes (Chart 2).

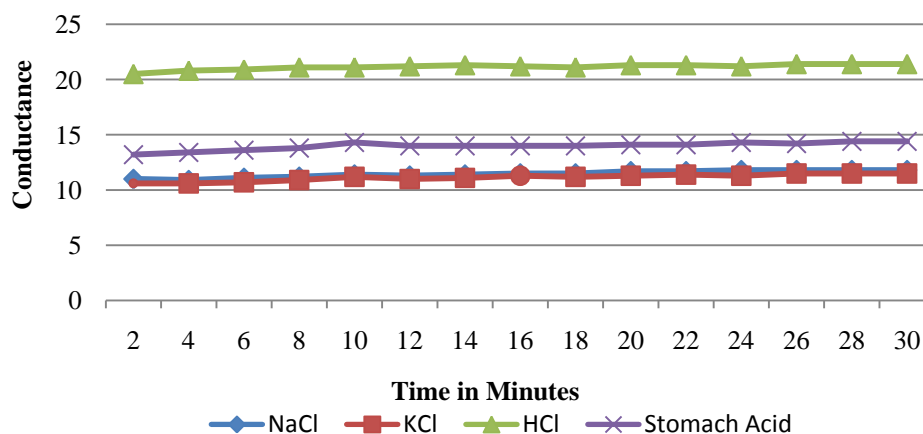


Chart 2 Conductance value of alprazolam.

For Librium, we carried out 15 cycles for NaCl, KCl, HCl and Stomach Acid. According to the readings, we plotted graph and found that conductance in NaCl is not changing significantly after 16 minutes.

In KCl, conductance didn't change after 16 minutes. In HCl, conductance didn't change after 18 minutes. In Stomach Acid, conductance didn't change after 16 minutes (Chart 3).

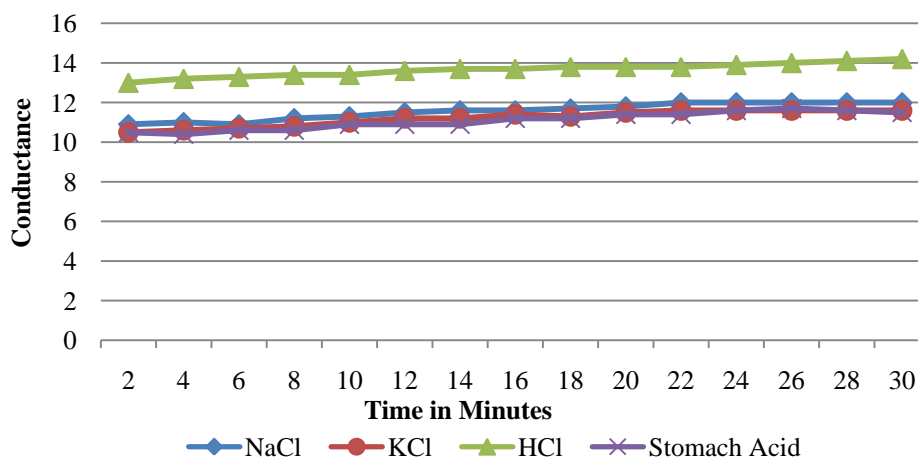


Chart 3 Conductance value of librium.

3.2 A Formula to Calculate

Calculation for drug solubility in stomach acid

$$S = \frac{K \times 1000}{\lambda m}$$

S = Solubility

λm = Molar Conductance

K = Specific Conductance

K = Conductivity observed \times Cell constant

3.2.1 For Diazepam

1) Specific Conductance Calculation

$$\begin{aligned} K &= 12.6 \times 10^{-2} \times 0.998 \\ &= 0.126 \times 0.998 \\ &= 0.1257 \end{aligned}$$

2) Solubility Calculation

$$\begin{aligned} S &= \frac{0.1257 \times 1000}{0.1236} \\ &= 1016.99 \text{ mg per litre} \end{aligned}$$

Therefore, Diazepam is soluble, 1 gm in 1000 ml. 0.05 gm in 50 ml.

3.2.2 For Alprazolam

1) Specific Conductance Calculation

$$K = 13.3 \times 10^{-2} \times 0.998$$

$$= 0.133 \times 0.998$$

$$= 0.1327$$

2) Solubility Calculation

$$\begin{aligned} S &= \frac{0.1327 \times 1000}{0.1398} \\ &= 949.2 \text{ mg per litre} \end{aligned}$$

Therefore, Alprazolam is soluble, 0.95 gm in 1000 ml. 0.0475 gm in 50 ml.

3.2.3 For Librium

1) Specific Conductance Calculation

$$\begin{aligned} K &= 10.6 \times 10^{-2} \times 0.998 \\ &= 0.106 \times 0.998 \\ &= 0.1057 \end{aligned}$$

2) Solubility Calculation

$$\begin{aligned} S &= \frac{0.1057 \times 1000}{0.1110} \\ &= 952.25 \text{ mg per litre} \end{aligned}$$

Therefore, Librium is soluble, 0.95 gm in 1000 ml. 0.0475 gm in 50 ml.

4. Conclusions

According to the conductivity findings, we can state the solubility of drug.

Solubility of Diazepam in stomach acid is 1 gm in 1000 ml. (0.05 gm in 50 ml.)

Solubility of Alprazolam in stomach acid is 0.95 gm in 1000 ml. (0.0475 gm in 50 ml.)

Solubility of Librium in stomach acid is 0.95 gm in 1000 ml. (0.0475 gm in 50 ml.)

Also, according to the conductivity findings, we can estimate time of dissolving.

Diazepam dissolves in stomach acid within 14-16 minutes.

Alprazolam dissolves in stomach acid within 12-14 minutes.

Librium dissolves in stomach acid within 16-18 minutes.

5. Discussion

Date rape drugs are drugs used to assist in a sexual assault, which is any type of sexual activity a person does not agree to. These are drugs are used as silent weapon that is being used to commit crime. These are generally tranquilizers. But due to its high usage, government placed these drugs under schedule. Due to unavailability of these conventional date rape drugs, criminals are searching for newer and easy available drugs. Generally a conventional date rape drug dissolves in stomach acid and starts their action within 30 minutes. But here in our study we found these alternative date rape drugs are more quickly soluble in stomach acid. That is alternative date rape drugs are soluble within 12 to 18 minutes. These alternative date rape drugs are generally available in white colored tablet which is odourless and tasteless. Hence it is very difficult to identify whether drug is mixed in drink or not. Through the discussion of this work we are proposing strict vigilance on production, administration and distribution of the tranquilizers. As these alternative date rape drugs are more quickly soluble and ultimately acts rapidly. This study can help to take presumptive rapid action if investigative agencies are get to know about date rape drugs are being administered to victim by accused unknowingly.

Investigator can also find out the time of administration of these date rape drugs. If deeper study of date rape drugs is carried out to create database of solubility, then it will be very helpful to investigative agencies to investigate the cases.

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References

- [1] Girard, A. L., & Senn, C. Y. 2008. "The Role of the New "Date Rape Drugs" in Attributions about Date Rape." *J Interpers Violence* 23 (1): 3-20.
- [2] Jansen, K. L. R., & Theron, L. 2006. "Ecstasy (MDMA), Methamphetamine, and Date Rape (Drug-Facilitated Sexual Assault): A Consideration of the Issues." *J Psychoactive Drugs* 38 (1): 1-12.
- [3] Abramowitz, M. Z. 2004. "GHB and Date Rape." *Br J Psychiatry* 185 (02): 176-7.
- [4] Calhoun, S. R., et al. 1996. "Abuse of Flunitrazepam (Rohypnol) and Other Benzodiazepines in Austin and South Texas." *J Psychoactive Drugs* 28 (2): 183-9.
- [5] Dressman, J. B., et al. 2007. "Estimating Drug Solubility in the Gastrointestinal Tract." *Adv Drug Deliv Rev* 59 (7): 591-602.
- [6] Mohler, H., Fritschy, J. M., & Rudolph, U. 2002. "A New Benzodiazepine Pharmacology." *J Pharmacol Exp Ther* 300 (1): 2-8.
- [7] Woods, J. H., & Winger, G. 1995. "Current Benzodiazepine Issues." *Psychopharmacology (Berl)* 118 (2): 107-15.
- [8] Kohrs, R., & Durieux, M. E. 1998. "Ketamine: Teaching an Old Drug New Tricks." *Anesth Analg* 87 (5): 1186-93.
- [9] Svenson, J. E., & Abernathy, M. K. 2007. "Ketamine for Prehospital Use: New Look at an Old Drug." *Am J Emerg Med* 25 (8): 977-80.
- [10] Hillestad, L., Hansen, T., Melsom, H., & Drivenes, A. 1974. "Diazepam Metabolism in Normal Man. I. Serum Concentrations and Clinical Effects after Intravenous, Intramuscular, and Oral Administration." *Clin Pharmacol Ther* 16 (3): 479-84.
- [11] Calcaterra, N. E., & Barrow, J. C. 2014. "Classics in

Chemical Neuroscience: Diazepam (Valium).” *ACS Chem Neurosci* 5 (4): 253-60.

- [12] Dawson, G. W., Jue, S. G., & Brogden, R. N. 1984. “Alprazolam: A Review of Its Pharmacodynamic Properties and Efficacy in the Treatment of Anxiety and

Depression.” *Drugs* 27 (2): 132-47.

- [13] Lorr, M., McNair, D. M., & Weinstein, G. J. 1963. “Early Effects of Chlordiazepoxide (librium) Used with Psychotherapy.” *Journal of Psychiatric Research* 1 (4): 257-270.