

# A tentative component analysis of Norjizak: A new abused drug in Iran

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**Abstract:** Norjizak is a new drug abused in the past few years in Iran with symptoms and complications distinct from other common forms of drug and characterized by higher rate of mortality. The present study aims to analyze the chemical components of this substance. Five samples were obtained from abusers referring from different areas of Tehran to a treatment clinic. All samples were 2ml vials with yellowish fluid. Thin Layer Chromatography (TLC) was performed first to analyze the samples semi-quantitatively and the quantitative levels of components were then explored using high-performance liquid chromatography (HPLC). TLC revealed steroid (in form of betamethasone), heroin, codeine, morphine and thebaine in all five samples. Four samples contained acetaminophen and two samples contained caffeine. None of them contained amphetamine, benzodiazepine, tricyclic antidepressant, aspirin, barbiturates, tramadol and buprenorphine. HPLC revealed that heroin, codeine, morphine and thebaine constituted the narcotic foundation in all samples. In addition, the heroin to acetylcodeine ratio was significantly lower in three samples, which indicates their higher toxicity. The results of the present study on the chemical components of Norjizak showed that this substance is an opiate one similar to heroin and the heroin-based crack prevalent in Iran which contains betamethasone.

**Keywords:** Narcotics, Norjizak, steroid, heroin, Iranian crack.

## INTRODUCTION

The diversity of narcotic substances is so wide today that certain drugs are specific to particular areas or regions only. Since these substances are produced illegally, and in many developing countries, hand-made, the components of each substance are exclusive to those areas. Norjizak, a name probably derived from Norgesic, is a hand-made injectable substance that has been abused in Iran for several years. Norgesic, or Norgesic Forte, is a brand name for a drug containing aspirin, caffeine and orphenadine citrate which is used for the symptomatic treatment of severe musculoskeletal pain and Parkinson's disease. This drug was first produced by Graceway and approved by FDA in 1964 (U.S. Food and Drug Administration). Temgesic is also a brand name for buprenorphine in injection form (The Pharma Guide). Although high dosage of these drugs can be lethal, no critical side-effects have been reported for their use. While Norgesic is found in the form of tablets, Norjizak is produced in the form of 2ml yellowish liquid vials in Iran and its neighboring countries of Pakistan and Afghanistan (Siavash *et al.*, 2009). Patients suffer from various side-effects depending on the dosage and length of addiction (Khourvash *et al.*, 2006). Since Norjizak is quite similar to the injectable formulation of buprenorphine, a drug used for the treatment of drug addiction in Iran and its severe edema (which is misconceived as weight gain and

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recovery for the addicts), not only many Iranian addicts were attracted to it, but it is also rarely prescribed for drug addiction treatment by some physicians. Although there is no official fig about the prevalence of Norjizak among Iranian addicts, addiction treatment practitioners report various side-effects such as abscess formation, septic emboli, soft tissue inflammation, avascular necrosis, and most notably Cushing's syndrome (Farhoudian *et al.*, 2011; Koushesh, Afshari & Afshari 2009; Siavash *et al.*, 2009; Azizi *et al.*, 2008; Kazemi *et al.*, 2007), which is indicative of steroid compound in this substance (Siavash *et al.*, 2009). In addition, this substance is so highly addictive that an average daily dosage of 7.5 vials by patients affected by Cushing's syndrome has been reported (Siavash *et al.*, 2009). On the other hand, its mortality rate is reported as 37.5% in some hospitalized intravenous drug abusers compared to addiction to heroin (17.9%) (Khourvash *et al.*, 2006). Since no study has been conducted on the chemical components of this substance in details to this date, the present study aims to analyze the chemical components of Norjizak using TLC and HPLC.

## MATERIALS AND METHODS

The present study was conducted at Bahar Toxicology Laboratory in Tehran. The authors could obtain only five samples from substance abusers around Tehran who were receiving treatment at different addiction treatment

centers. All samples included yellowish liquid vials (fig. 1). None of the vials were labeled or otherwise identified. Two vials contained transparent liquid without any suspension (normal vials) and two had solid particles that had deposited like sugar that stuck together and to the vials. This type of liquid is known as "Shekari" ("sugary") by Norjizak abusers. Another type of liquid, which is recognized as "Doughi" ("yogurt in water"), contained fine white particles that either did not dissolve so loose that could roil easily at the faintest shake.

To analyze the chemical combination of Norjizak, first the samples extracted by means of 99% chloroform solution. The extracted Norjizak samples with 5% (1/20) concentrations and at 23-28°C were then centrifuged at 13,000 rpm for 10 seconds to separate the impurities. The upper phase solution was then scaled through thin layer chromatography (TLC) and high-performance liquid chromatography (HPLC). TLC was performed for the semi-quantitative analysis of the samples for the reference compounds shown in table 1. HPLC was then performed to analyze quantitatively those compounds which were revealed through TLC. The samples were injected into a Japan-made Shimadzu analyzer (SDP-10A-VP) containing methanol, acetonitrile and bisphosphonates at the flow rate of 1 ml/m and a volume of 20 micro liter and were analyzed with 210-nm UV light. The HPLC column was made of C18 resin. The methanol and chloroform standards and buffers were made by Merk (Germany) or Romil (England). The heroin sample standard was procured from T&H SMITH Ltd., the tramadol sample from Tehran Pharmaceutical Company and remaining standards were procured from Iranian Temad Company. Since there was no standard sample available for acetylcodeine (6-monoacetylc morphine), its concentration was calculated indirectly by division of the heroin (diamorphine) under the curve area to the under the curve area of acetylcodeine and multiplying the result by the heroin concentration. The data were analyzed by Autochrome v.1, 2000.

**Table 1:** Reference compounds used in TLC

	Substance	Sensitivity
1	Morphine, Heroin, Codeine, Thebaine, Cannabis	300 ng/ml
2	Methadone, Buprenorphine, Amphetamines, Cocaine	500 ng/ml
3	Tramadol, Aspirin, Acetaminophen, Diphenoxylate, Benzodiazepines, Trihexyphenidyl, Biperiden, Tricyclic antidepressants	1 µg/ml
4	Steroids (Betamethasone, Dexamethasone, Hydrocortisone)	1 µg/ml
5	Caffeine, Barbiturates	5 µg/ml

## RESULTS

Table 2 shows the results obtained for different compounds in the Norjizak samples using TLC. As can be seen, all samples contain steroid (in form of betamethasone not dexamethasone or hydrocortisone), heroin, codeine, morphine and thebaine. In addition, four samples contained acetaminophen and two contained caffeine. None of them contained amphetamine, benzodiazepine, tricyclic antidepressant, aspirin, barbiturates, tramadol and buprenorphine.

Fig. 2 shows quantitative analysis of sample no 3 by HPLC. Table 3 and fig. 3 present the quantitative analysis results of Norjizak samples using HPLC. As can be seen, heroin, codeine, morphine and thebaine constituted the narcotic foundation in all samples and most samples also contained a significant concentration of acetylcodeine. Fig. 4 shows the heroin to acetylcodeine ratio in all samples.

## DISCUSSION

The present chemical analysis of Norjizak revealed that this substance is a narcotic substance constituting heroin, codeine, morphine, thebaine, acetaminophen and a significant concentration of acetylcodeine which has steroid (in form of betamethasone). None of the samples contained stimulants such as cocaine, drugs and impurities such as tranquilizers (benzodiazepines and Phenobarbitals), tricyclic antidepressant, aspirin or other synthetic narcotics (e.g. tramadol and buprenorphine). These differences distinguish Norjizak from Norgestic.

The chemical analysis of Norjizak showed that it may originate from the opium poppy (*Papaver Somniferum*) as all samples contained heroin, morphine, thebaine and acetylcodeine. In addition, none of the samples contained buprenorphine. Therefore, one should rule out Norjizak as a new name adopted for buprenorphine, formerly traded in Iran with the brand names of Temgesic, Duragesic and recently Norgestic. The chemical combination of Norjizak abused in Iran has strong resemblance to the Iranian crack (or *Kerack*), which is a heroin-based prevalent drug in Iran (Kazemifar, Solhi & Badakhshan 2011), except for its additional corticosteroid. The constituent steroid may account for different clinical symptoms of this drug (including weight gain, increased appetite, edema and weakened immunity system) compared with other opioid drugs (Siavash *et al.*, 2009). The type of corticosteroid found in our samples was betamethasone. However, in their study on 30 patients abusing Norjizak diagnosed with Cushing's syndrome, Siavash *et al.*, asserted the corticosteroid to be of dexamethasone type (Siavash *et al.*, 2009). In addition, in Azizi *et al.*, study, who reported some cases of exogenous Cushing's syndrome due to unlicensed medications, the used substances were 2 ml

vials named Temgesic. However, vials had substantial amount of dexamethasone without any amount of buprenorphine (Azizi *et al.*, 2008). Although in these two studies betamethasone was not used as comparison corticosteroids, the existence of dexamethasone in their analysis indicates the diversity of corticosteroid types used in the production of this hand-made drug in different geographical areas. In addition, Siavash *et al.* used gas chromatography-mass spectrometry (GC-MS) in their study while we used the HPLC method. It appears that through dishonest claims about Norjizak as a medication for the treatment of addiction to drugs such as opium or heroin, drug traffickers deceptively used corticosteroid compounds which cause physical swelling and facial puff (symptoms of Cushing's syndrome) and false weight gain to deceive the addicts and their families about the treatment. The fact is, however, that the steroid contained in this substance has numerous adverse side-effects which may lead to the patient's death. However, the abuse of Norjizak has significantly dropped due to severe side-effects, widespread mortality and effective and aggressive anti-drug campaigns by police. Although there is no official report on the abuse of this substance in Iran, informal accounts by addiction treatment practitioners show a significant decrease in its use.

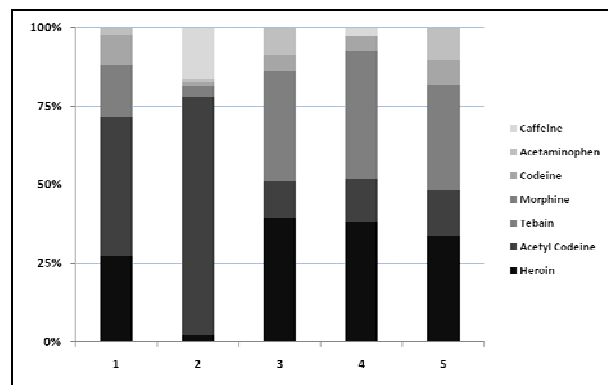


**Fig. 1:** Picture of one Norjizak vial.

Steroid is not the only dangerous compound found in Norjizak. As the results showed, the proportion of heroin to acetylcodeine was low in three samples, which implies that this substance is severely toxic because of the inadequate driving of heroin from morphine. When in human body, acetylcodeine metabolizes into codeine and then to morphine whose overdose causes undue release of histamine in the blood which may lead to anaphylactic shock, convulsion or even death (O'Neal, Poklis & Lichtman 2001). This may explain the higher mortality caused by addiction to Norjizak injection (37.5%) compared to addiction to heroin (17.9%) (Khourvash *et al.*, 2006). The highly addictiveness of Norjizak abuse could also explain its high mortality among addicts, since self-reported doses show an average of 7.5 vials in a day

(Siavash *et al.*, 2009). In addition, using unsterilized instruments may cause various infections such as fungal infections, endocarditis and infectious meningitis (Khourvash *et al.*, 2006).

Contrary to Siavash *et al.*, in our study we did not find buprenorphine and benzodiazepines as constituent compounds of Norjizak (Siavash *et al.* 2009). Although in their study they referred to Norjizak as their study drug abused by patients, the fact that buprenorphine was not found in our study on Norjizak and also the fact that Temgesic can also be used in injection formulation may imply that Siavash *et al.* had studied Temgesic, which contains buprenorphine as a foundation compound. Although the samples in their study were not fully described, it appears that they found corticosteroid in their Temgesic samples (Siavash *et al.*, 2009). In addition, anecdotal experiences by addiction treatment practitioners are in favor of early symptoms caused by buprenorphine and steroid compounds although buprenorphine is shortly afterwards replaced by heroin. Therefore, Siavash *et al.* might have used a combination of old and new samples of Norjizak in their study. On the other hand, none of samples in Azizi *et al.*, study, which the addicts entitled them as Temgesic, had buprenorphine (Azizi *et al.*, 2008). These controversies about chemical constituents of Iranian hand-made Norjizak and/or Temgesic could explain by changes in their production over time. Hence, knowing the chemical components of such substances in any time could help patients for better diagnosis and treatment.



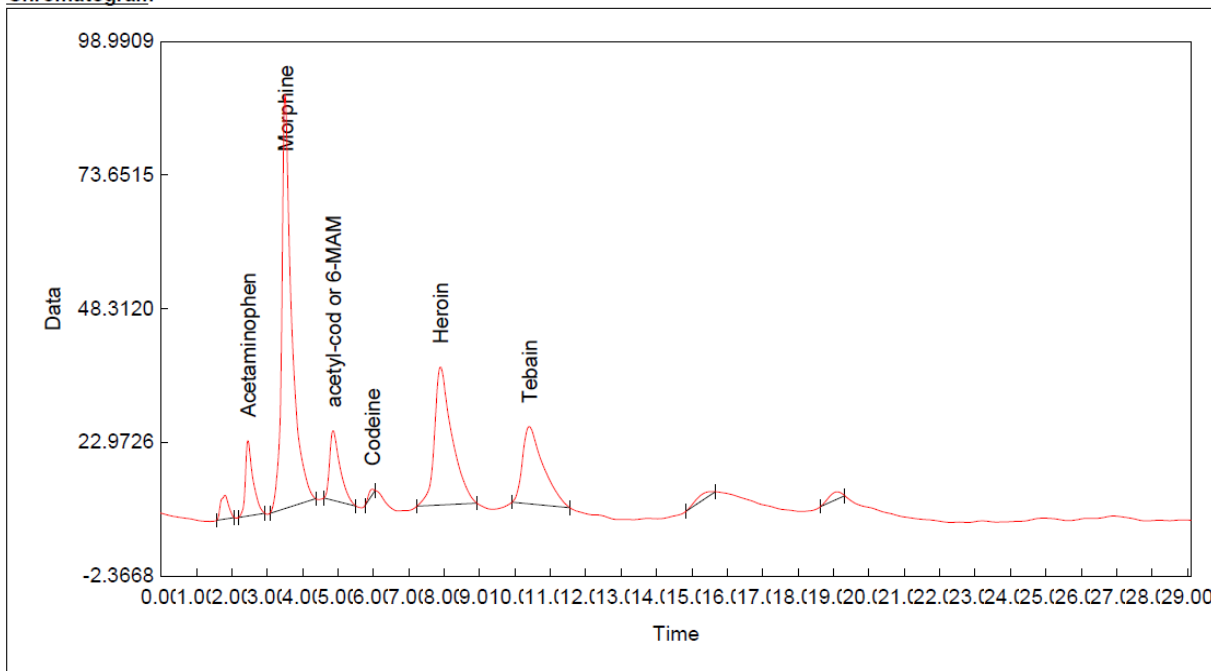
**Fig. 3:** Percentage of chemical components of Norjizak samples in HPLC.

Since no orphenadrine standard (the principal compound in the European Norgesic) was available at the time of study, we cannot make any claim whether or not it exists in the Iranian Norjizak. Nevertheless, the absence of aspirin and the existence of significant concentrations of opioid compounds in the Iranian Norjizak ensures us that the Iranian Norjizak is quite different from the original Norgesic (containing orphenadrine, aspirin and caffeine) which is further confirmed by the highly addictiveness of the Iranian Norjizak.

**Analysis Information**

File Name : 1094.raw  
 Sample Name : sam-21-1/20-ph7-ng/ml  
 Analysis Time : 22/ 02/ 2009 17: 47: 24  
 Print Time : 7 / 8 / 2010, 17 : 19 : 3

**Chromatogram**



**Result**

Num	RT[min]	Peak	Area[mV*s]	Width[sec]	Concentration[ng/ml]
1	1.8067		71.8545	30.5000	0.0000
2	2.4517	Acetaminophen	213.6950	44.5000	9.7807
3	3.5000	Morphine	1564.0198	77.5000	24.9253
4	4.8567	acetyl-cod or 6-MAM	274.1282	54.4000	0.0000
5	5.9550	Codeine	13.2137	17.7000	5.7946
6	7.8883	Heroin	924.7478	101.5000	44.4886
7	10.3883	Tebain	610.6560	97.5000	14.7586
8	15.5250		36.5589	49.5000	0.0000
9	19.0700		37.1705	40.5000	0.0000
Sum			3746.0444		99.7478

**Fig. 2:** Results of quantitative analysis of sample no 3 by HPLC.

This is one of a few studies that analyze the chemical combination of an abused Iranian drug. Such studies could lead to know new substances for facilitating and better treatment management. However, this study is limited by the few number of samples utilized which is due to significant drop in its use (caused by severe side-effects and high mortality rate). What makes the study further limited is the fact that the samples were collected from Tehran only while this substance originates from Eastern areas of Iran near the Afghanistan and Pakistan

borders. Nevertheless, since Norjizak is a hand-made substance it would be likely that the foundation compound remained the same even if more and wider samples were analyzed. However, different types could vary in the concentration levels of their constituent compounds as was evidenced in our five samples. Unavailability of an orphenadrine standard was another limitation which prevented us from comparing this substance with the typical Norgesic.

**Table 2:** TLC results of Norjizak samples

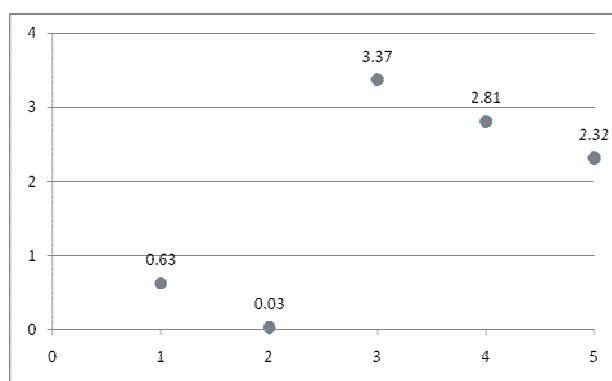
Sample No.	Morphine	Codeine	Heroin	Thebaine	Methadone	Cocaine	Tramadol	Diphenoxylate	Trihexyphenidyl	Biperiden	Amphetamine	Benzodiazepines	Tricyclic antidepressants	Aspirin	Caffeine	Phenobarbital	Acetaminophen	Buprenorphine	Steroids		
																			Betamethasone	Dexamethasone	Hydrocortisone
1	+	+	+	+	-	-	-	-	-	-	-	-	-	-	+	-	-	-	+	-	-
2	+	+	+	+	-	-	-	-	-	-	-	-	-	-	+	-	+	-	+	-	-
3	+	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	-
4	+	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	-
5	+	+	+	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	-

**Table 3:** HPLC results (ng/ml) for quantitative concentration of chemical compounds in Norjizak samples

Sample No.	Heroin	Acetaminophen	Caffeine	Morphine	Codeine	Thebaine	acetyl-codeine (6-Mono Acetyl Morphine)*	Dia-morphine/ Acetyl codeine under the curve area**
1	53.59	4.62	0.00	12.40	18.87	19.75	85.70	0.63
2	11.17	4.57	72.78	7.55	5.67	8.76	338.22	0.03
3	44.49	9.78	0.00	24.93	5.79	14.76	13.19	3.37
4	52.58	0.00	3.62	41.99	6.41	14.25	18.70	2.81
5	33.40	10.17	0.00	19.32	7.74	13.56	14.40	2.32
Min.	39.04	5.83	15.28	21.24	8.90	14.21	94.04	1.83
Max.	11.17	0.00	0.00	7.55	5.67	8.76	13.19	0.03
Mean	53.59	10.17	72.78	41.99	18.87	19.75	338.22	3.37
SD	17.56	4.23	32.18	13.36	5.64	3.91	139.87	1.44

\*Concentration calculated indirectly through dividing the under curve area of heroin by the under the curve area of acetylcodeine and multiplying the result by the heroin concentration.

\*\*Proportion of under curve area of heroin to the under the curve area of acetylcodeine (no unit).

**Fig. 4:** Heroin to acetylcodeine ratio in Norjizak samples.

## CONCLUSION

The results of our chemical analysis of Norjizak indicate that this substance is a heroin-based drug, similar to the heroin and heroin-based crack (*Kerack*) abused in Iran, containing steroid in form of betamethasone.

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