# Introduction

Almost any substance has the potential for abuse which is defined as voluntary intake to the point of causing physical or psychological harm. Drug abuse is a serious social problem throughout the world. During the past two or three decades, in addition to classic drugs such as morphine, cocaine and marijuana, chemically synthesized drugs, so-called designer from controlled drugs, have became spread in many countries. Among these compounds, fentanyl and pentazocine are widely abused, Higashi Kawa and Suzuki (2008).

In forensic science practice, the identification and quantification of a chemical (s) are essential in case of victims whose cause of death is considered to be related to intoxication with drugs or poisons. The main interest in this field is being focused on methodologies of how rapidly, accurately and sensitivity the chemicals can be detected, this field is called forensic analytical toxicology and is highly dependent on development of new analytical techniques or instruments.

The interpretation of analytical results is often the most difficult aspect of forensic analytical toxicology; the interpretation of drug concentrations is dependent on a number of variables that can result in anatomical site differences of blood levels and changer over the time. The goal of interpreting postmortem drug concentrations is to determine whether the drugs measured may have played a role in the cause of death, Leikin and Watson (2003).

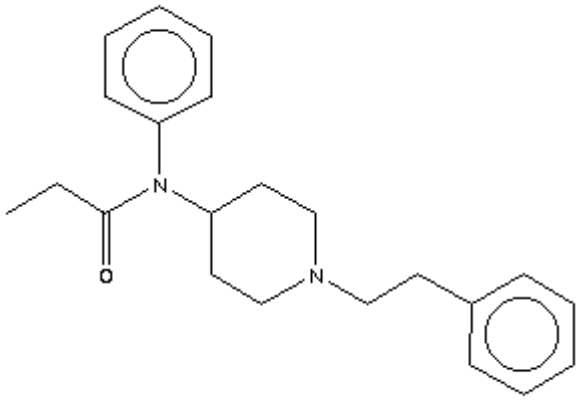
Drug concentrations obtained from postmortem samples do not necessarily reflect the blood concentration at the time of death due to variations according to the sampling site and the interval between death and sampling. These site and time dependent variations have been attributed to a multifaceted process occurring after death, termed as postmortem redistribution (PMR). The high complexity of PMR process is amplified by the fact that it does not refer exclusively to fatal poisoning, but it may also reflect antemortem behavioral effects as well as the integrity of cellular membranes is lost after death, hollow organs, such as different parts of gastrointestinal tract or viscera with high concentrating power, such as liver, lung and heart can function as drug reservoirs. Also, the particular

pharmacokinetic properties of certain drugs may in turn lead to alterations in dug concentrations.

Biotransformation of drugs by metabolizing enzymes could also be triggered in early steps of postmortem period. Thus, PMR of drugs may complicate the interpretation of the analytical results in forensic toxicology and has emergently been considered as “a toxicology nightmare”, Giaginis *et al.,* (2009).

The dangers of opioid overdose have been recognized for as long as the use of opium itself. In a number of countries, the use of heroin and other opioids in medical and non-medical contest is associated with an increasing rate of overdose, white and Irvine (1999). Fentanyl and pentazocine are two of the medical used opioids and are abused, these two drugs which we will focus on in this study.

Fentanyl, or N-Phenyl-N-[1-(2-phenylethyl)-4-piperidinyl] propanamide , USP 27,( 2004) was originally described by Janssen in 1959 and is still among the most important drugs.




Fentanyl acts primarily as a pure and selective opioid μ receptor agonist that relives pain with fewer adverse effects and more potent analgesic effect than morphine, and because of its strong sedative properties, it has become an analogue of illicit drugs such as heroin. Its unambiguous detection and identification in environmental samples can be regarded as strong evidence of its illicit preparation, Gupta *et al.*, (2007). It is used in surgical anesthesia as it is yet up to 200 times more potent than morphine, Moore *et al.*, (2008). It was introduced in clinical practice in 1960s as an analgesic and its application as an aesthetic agent reflects it's much greater potency than other contemporary opiate agonists, Gupta *et al.*, (2007).

Fentanyl is administrated via intravenous, intramuscular, epidural, transdermal and transmucosal routes. It is found in many forms as injection

ampoules, patches and even a flavored-lollipop of fentanyl citrate mixed with inert fillers on a stick.

Janssen pharmaceutical reached record profits of over a billion dollars gross sales of fentanyl in 2004 following prescription practices extending beyond chronic cancer and non-cancer malignant pain. So more recently, they developed an effervescent fentanyl tablet for buccal absorption, followed by a buccal spray device and other delivery methods currently in development (Barr Pharmaceutical, 2008).

Many reports of toxicological findings of fatal fentanyl intoxication due to ingestion of transdermal patches (Marquardt and tharratt 1994; Kramer and Tawney, 1998; Choi *et al.*, 2001; Snell *et al.*, 2002; Baselt 2004; Coon *et al.*, 2005; Hughes *et al.*, 2005, Miller *et al.*, 2005; Teske *et al.*, 2007; Woodall *et al.*, 2008; and Firestone *et al.*, 2009 ).

Also, fentanyl intranasal formulations caused intranasal toxicity,

Ran Klove *et al.*, (2006). In addition, fentanyl theft has been reported from nursing homes and other long-term care facilities, recently, clandestine production and distribution of fentanyl powder and tablets have also surface, (Regnard and Pelham, 2003; and Gupta *et al.*, 2007). In the first half of 2006, clandestinely produced samples leading to more than 100 overdoses and deaths in heroin addicts in illinois, Michigan, Ropero- Miller, (2006), also, in other states of USA , Fodale *et al.*, (2008).

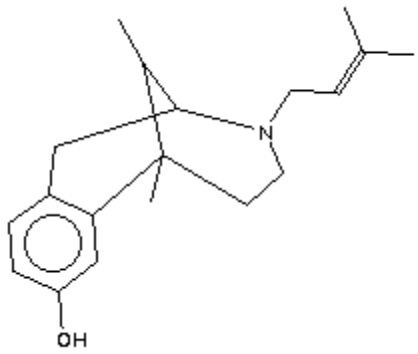
In sweden during a 16-month period, nine fatalities occurred amoung white male-drug addicts where fentanyl was detected at postmortem toxicological analysis. As the street samples associated with these cases confirmed the presence of fentanyl in low-concentration amphetamine powders in seven of these cases, an acute intoxication by fentanyl was considered to be the immediate cause of death, Kronstrand *et al.*, (1997).

Moreover, between september 2005 and april 2007, 350 fentanyl intoxication deaths were inrestigated and certified by the cook county, Denton *et al.*, (2008). In Toronto Canada, fentanyl is a highly desired,

sought after and relatively expensive prescription opioids drug among street users, FireStone *et al.,* (2009).

Pentazocine, a synthetic benzomorphan derivative, is widely prescribed as a potent analgesic drug, and has received attention in forensic toxicology in relation to addiction or fatal intoxication, as there are many cases of pentazocine abuse especially for medical co-medical workers, (Challoner *et al.*, 1990; Ryall and stumpers, 1991; Portenoy and Payne, 1992; and Imamura *et al.,* 1999).

Pentazocine or 2,6-Methano-3-benzazocin-8-ol, 1,2,3,4,5,6-hexahydro-6,11-dimethyl-3-(3-methyl-2-butenyl)-, (2α,6α,11R*) (USP 27, 2004).



Pentazocine was introduced in 1967 as a “non narcotic, non addicting” analgesic. However, the abuse potential of this medication was soon recognized, (Kim And song, 1996 ; Jain *et al.*, 1999; and Agarwal and Trivedi, 2007).

In the 1970s, recreational drug users discovered that combining pentazocine with tripelennamine (a first-generation ethylenediamine antihistamine) produced a euphoric sensation much like that brought by heroin. Users who were already addicted to heroin oftenused this combination when heroin was unavailable to them. It is commonly asserted that the use of pentazocine with tripelennamine originated among development is that pentazocine is combined with methyl phenidate (Ritalin) via the oral route or insufflations.

Pentazocine is a short acting narcotic-antagonist analgesic and has been used in the management of patients with post-operative pain or initial carcinogenic pain, Wada *et al.,* (2007). Development of matrix controlled trans dermal delivery systems of pentazocine: In vitro/ In vivo performance,

(Portenoy and Payne , 1992; Brown *et al.,* 2006; Furuishi *et al.*, 2007 and Verma *et al.,* 2009).

In Taiwan, pentazocine is a widely abused narcotic analgesic drug that frequently combines with morphine or tripelennamine to produce heroin like effects, Chan *et al.,* (2007).

In a retrospective study of surgical neonates who received analgesia with pentazocine between January 1998 and December 2007 fifteen patients were identified who subsequently developed respiratory depression and died, Osifo and Aghahow, (2008).

Also, pentazocine caused tonic-clonic seizure in patients, Okamoto *et al.,* (2008). Reports on the analysis of fentanyl and pentazocine have been published, but most focused on the determination of the drug in biological fluids such as plasma, cerebrospinal fluid, urine ect.

In forensic toxicological examination, fresh body fluids are not always available because putrefaction, degradation and contamination have often

occurred. Even whole blood cannot always be obtained owing to hemorrhage, so, the need of applying sensitive, selective and reliable methods, applicable to both detection and determination of both fentanyl and pentazocine in solid tissues such as liver, brain, muscle, kidney, hair, spleen and biological fluids such as blood. Also, studying the effect of putrefaction on the drugs stability in tissue and determine which organ will be of choice in having the highest concentration and long duration of drug stability in case of putrefied tissues.

**In summary, the present work is an attempt to:**

1- Employ the different toxicological analytical procedures (spot tests), TLC, UV spectrophotometry and GC to reveal which of these methods or all together more suitable for the identification and differentiation of the two studied drugs, fentanyl and pentazocine.

2- Estimation the postmortem drug concentration in some tissues of rat injected different doses of the drug. Also, It is aimed to demonstrate the effect of putrefaction on the drug stability and identification and also to define the time at which the drug disappear in such putrefied tissues.