Turkish Journal of Agricultural and Natural Sciences
Special Issue: 2, 2014

TÜRK
TARIM ve DOĞA BİLİMLERİ
DERGİSİ

TURKISH
JOURNAL of AGRICULTURAL
and NATURAL SCIENCES

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Therapeutic and Toxic Effects of Alkaloids Extracted of Somnniferum Papaver

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Abstract

The wealth of their contribution to every painful or dangerous hour of the life of the man gives to the plants a choice place in the social representations. Nowadays in spite of the development of the chemistry of synthesis, the use of the medicinal herbs preserved a broad place because of their effectiveness in various therapeutic procedures thanks to their active ingredients which they contain. The opiates are the psychotropic substances resulting from the poppy with opium: Papaver Somniferum, a plant known since more than four thousand years before J-C. The Greek doctor Galien prescribed opium in a receipt against various evils (cough, headaches, deseases of the gall bladder), after it was consumed as euphoriant from the 19th century. Opium is the latex exuded by the capsules of the poppy, it contains about thirty different alkaloids from which the structure is derived of phenanthrene (morphine, codeine, thebaine,…),or derived of isoquinoleine (papaverin, narcotin, narceine,…).Morphine is the most abundant alkaloid of the opium which contains 10% of them, this value can vary the simple one with the double according to the producting regions, it is also the most active alkaloid and that whose properties are searched by the opium addicts. In this context, the main aims of this work were to demonstrate the method of extraction,separation and identification of alkaloids of opium (opiates) and to study the therapeutic and toxic effects of alkaloids extracted of opium.

Keywords: opiates, morphine, codeine, analgesics, alkaloid, psychotropic.

Introduction :

The analgesics are drugs intended to remove the painful feelings, without deterioration of the other feelings (tactile, auditive, and visual) nor modification of the conscience. One distinguishes the analgesics classically not morphine “analgesics peripheral nonnarcotic), whose action is exerted on the level of the painful site, by inhibition of prostaglandin synthesis, although central effects were also highlighted, some of these compounds are anti-inflammatory drugs and antipyretic, and the central or morphine analgesics “major narcotic analgesics” whose action is exerted by inhibiting integration on the level of the cerebral cortex of the painful stimuli, they also depress the transmission of the noxious messages at the spinal level and the cerebral trunk. Into therapeutic, they are employed mainly in the treatment of the intense pains, of traumatic origin, post-operative or cancerous.

Oldest of the active ingredients used in this field is morphine, known since antiquity, the direct analogues saw the day, such as the hydromorphone, the oxymorphone. By simplification of the polycyclic structure derivatives of Morphinane 1950 and benzomorphane 1960 appeared. Later, agonists and/or antagonists such as Nalorphine, Nalbuphine, Naloxone 1959 - 1968 and of the more complex analogues Buprénorphine 1968 were introduced into therapeutic.

n parallel, non-polycyclic structures revealed an activity analgesic power station: Derived pethidine 1939, Fentanyl and 1963 – 1990. From the years 1980, the description endogenous peptide opioids (B-endorphins and proenképhalines) and more recently that of tétrapeptides endogenous agonists of the receivers u (endorphins 1 and 2), as well as the best knowledge of the mode of action of the central analgesics, made or not develop many analogues of

peptide structure, agonists or antagonists of the concerned receivers.

Morphine: Morphine is the most abundant opiate found in opium , the primary source of morphine is chemical extraction from opuim. The composition of latex comprises following alkaloids: morphine 9 -10%, narcotin 5%, papaverin 0.8 – 0.9%, thebaine 0,4%, codeine 0.3 – 0.4% and narceine 0.2%.

Morphine is produced most predominantly early in the life cycle of the plant. Past the optimum point for extraction, various processes in the plant produce codeine, thebaine , and in some cases negligible amounts of hydromorphone , dihydromorphine , dihydrocodeine , tetrahydro-thebaine, and hydrocodone .

Figure 1. Capsules and flowers of the poppy (Pappaver somniferum).

○ Chemical structure: Pentacyclic structure deriving from Morphinane comprising 5 cycles of which a cycle piperidin and a cycle furan, it has 5 centers of chirality, from where 32 stereophony-isomers corresponding to 16 couples of antipodes.

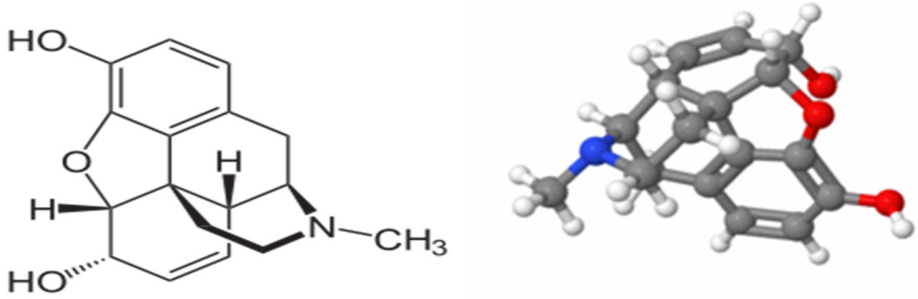

Figure 2. Chemical structure of Morphine.

Relation structure-activity : Morphine (+) is inactive and only the laevogyrous isomer Morphine (-) has the properties analgesics, the suppression of the cycle D of Morphine led to the loss of the antalgic activity, Morphine with the physiological pH is in form ionized on the level of the group N-methyl (active form). Alkylation gives the Codeine witch have a very weak affinity, Stage II, used as moderated, sedative analgesic of cough, the diacetylation gives Heroin more analgesic, toxicomanogene and illucit, various agonists are obtained by Substitution of the hydroxyls groups (OH) of morphine.

The human body produces endogenous opioid peptides that function as neurotransmitters and have similar chemical structure and effects of Morphine, endogenous opioids include endorphins, enkephalins , dynorphins , and even morphine itself.

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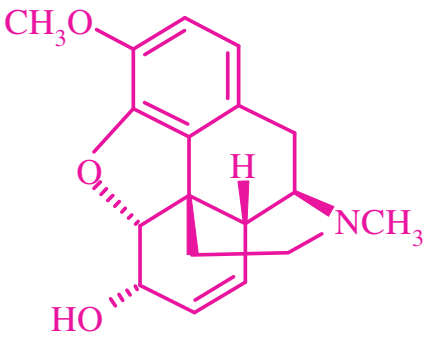

Figure 3. Chemical structure of codeine.

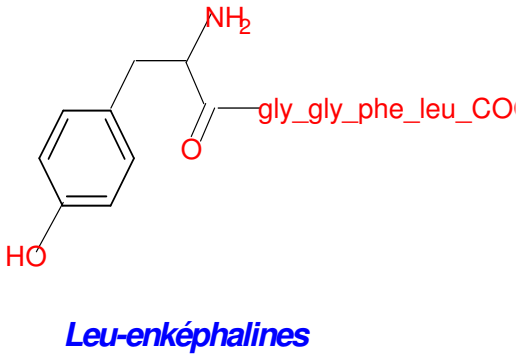

Figure 4.endogenous opioids.

- Method of extraction: Morphine is obtained by extraction starting from the opium extracted the capsules of poppy (Papaver somniferum) or it is beside other alkaloids with the state of salts (lactates, méconates, sulphates). Morphine (-) activates is extracted in several stages then, it is purified, the cost price is less low than that of its preparation by total synthesis.

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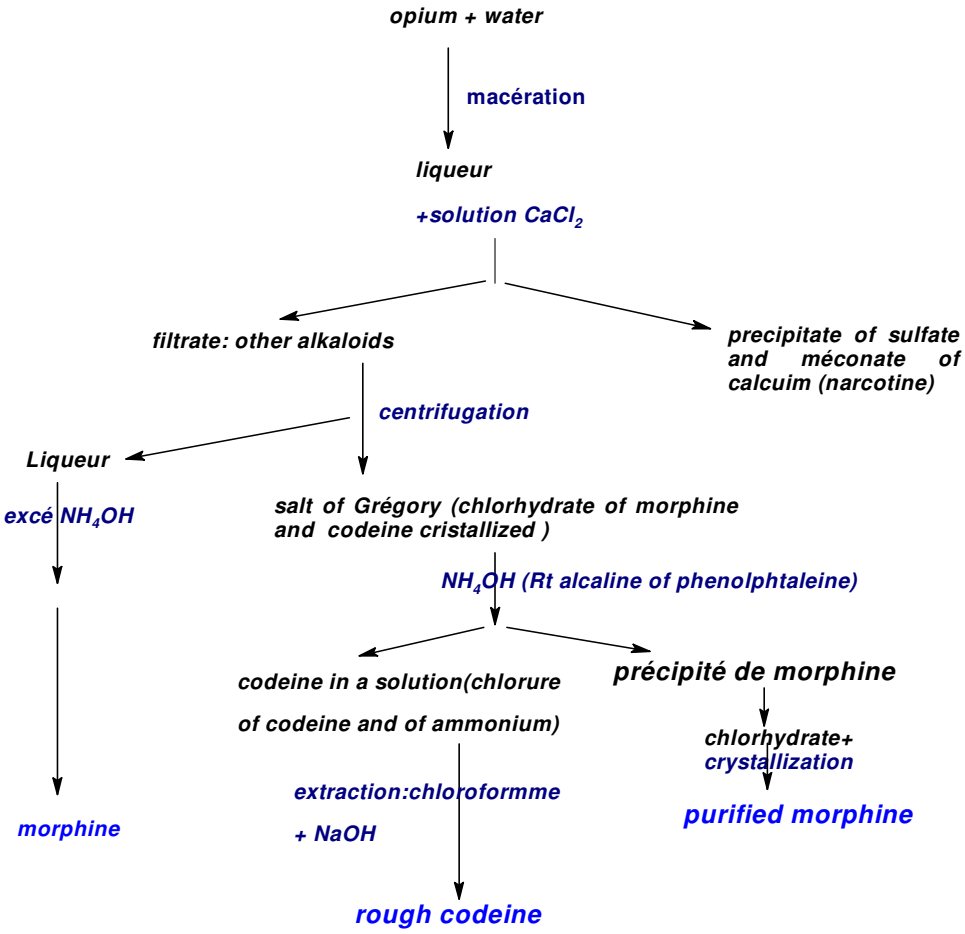

Figure 5. Method of extraction of Morphine.

o Mecanism of action: Synergy of two effects mono- aminergique effect inhibit recaptures of serotonin implied in the control of the nociceptive transmission and effect opioid agonist driven extremely inhibit the transmission of the doulourous impulses while fixing itself on the receivers opioids driven Mu, Morphine is agonist selective for receivers Mu than for receivers Kappa and delta.

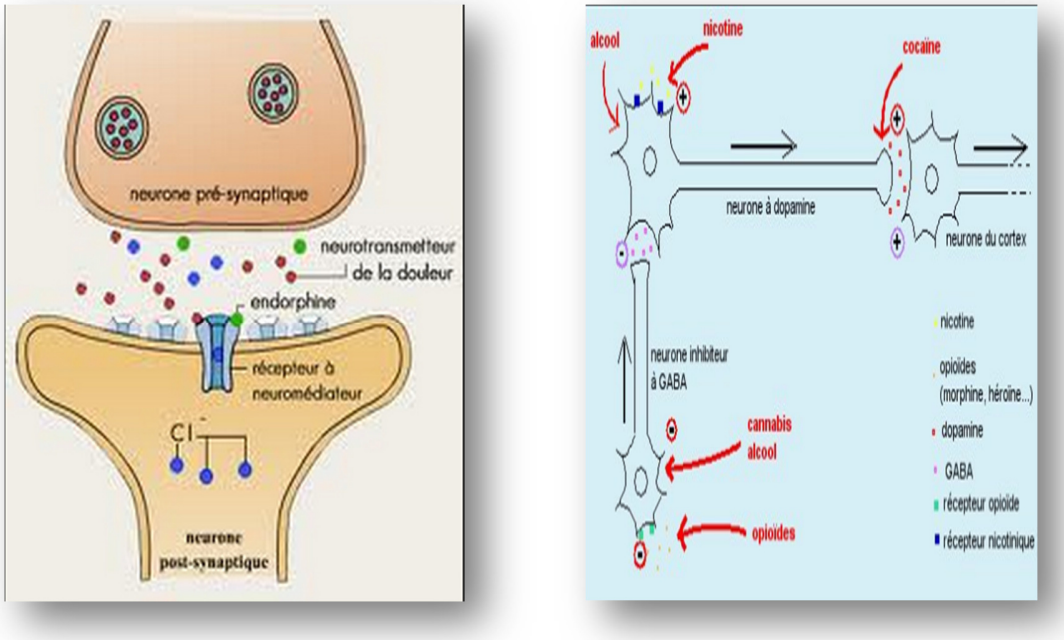

Figure 6. Mechanism of action of Morphine

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o Indications: Analgesic drug in intense pains, fast action by I.V, calming agitation The antalgic effect is amount depending and without levelling off, Its duration of analgesia is about 3–4 hours when administered via the IV, SC, or IM route and 3–6 hours when given by mouth.

o Undesirables effects: Nauseas, vomiting, constipation, respiratory depression, tolerance and dependence.

o Toxicity: hypnogene effect, somnolence, constipation, nauseas, vomiting.

Structural Morphine analogues:

Structural modifications were carried out by N-alkylation, oxydation in position 6 or by cyclisation of Morphine in order to get:

- partial agonists: Buprenorphine
- complete agonists: Oxycodone, Hydromorphone
- antagonists : Naloxone, Naltrexone
- agonists - antagonists: Nalorphine, Nalbuphine.

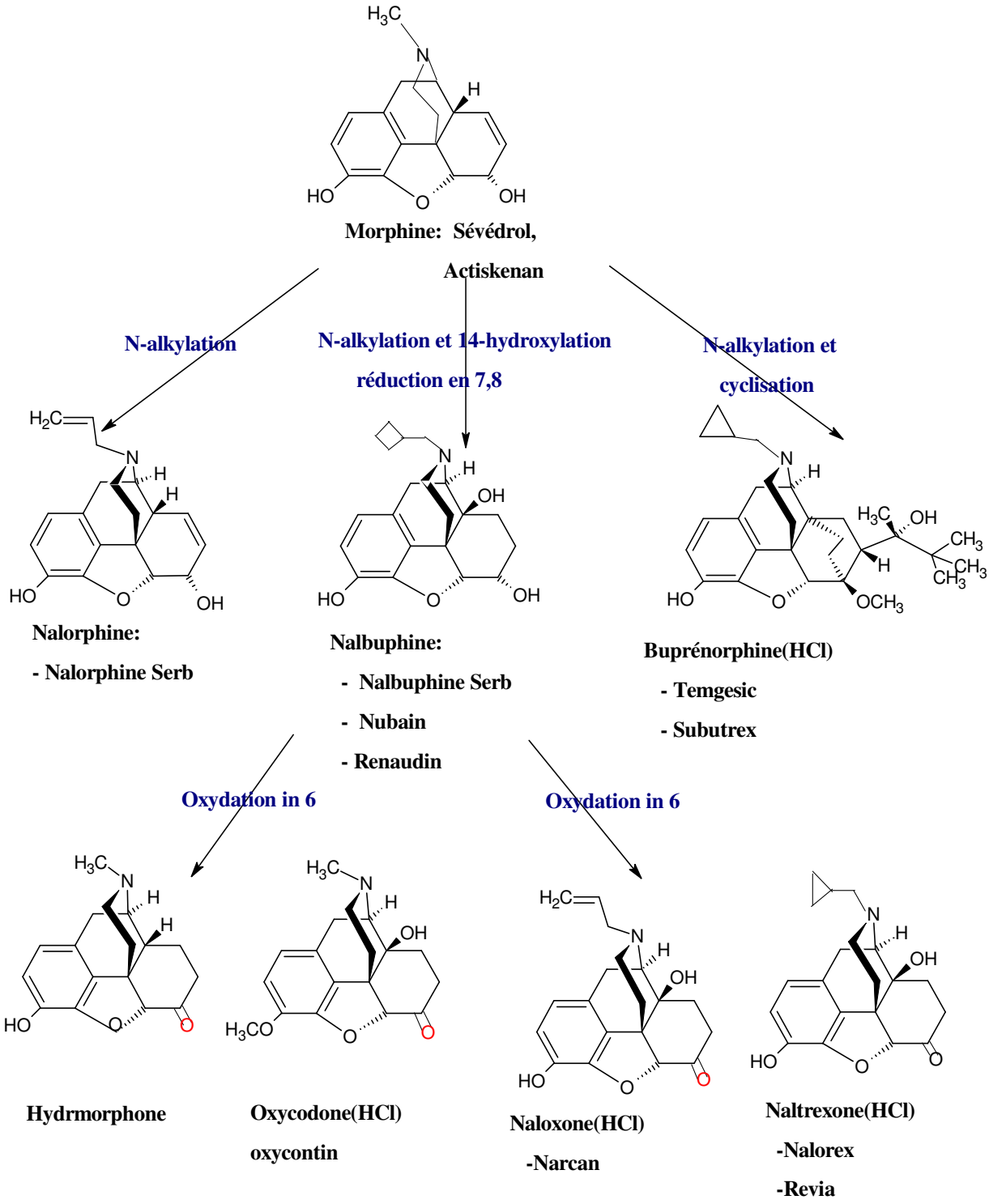

Figure 7. Strutural Morphine analogues hemisynthetic.

Buprenorphine : N-cyclopropylméthyl drift of the oripavine (alkaloid of various poppies), it acts by connection with the receivers driven (u) responsible for the analgesics effects and connection with the receivers kappa and delta responsible for the antagonistic effect. The connection with the receivers (u) is slower to be established than with Morphine; but once this connection is made, it lasts longer, it is thus a analgesics more powerful than the Morphine and of action prolonged with a decreased risk of syndrome of weaning. It is a substitution therapy at the drug addict, by parenteral way 0.3 Mg of Buprénorphine corresponds to 10 Morphine Mg

Other Structural modifications were carried out by suppression of cycles of Morphine in order to get simplified analogues: Péthidine, Fentanyl.

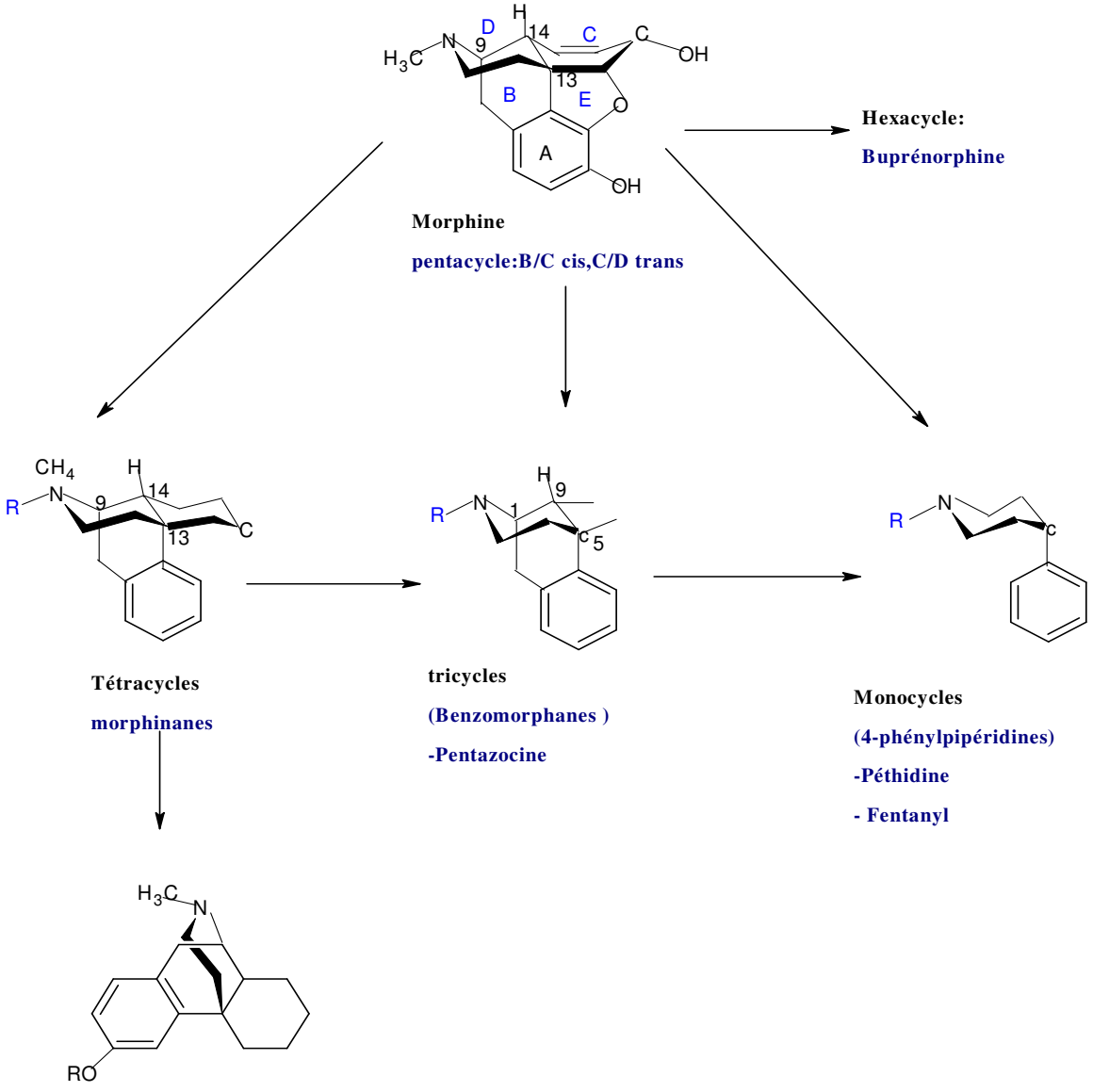

Figure 8. Simplified analogues of Morphine.

- Fentanyl : analgesic more powerful than morphine (80 X more), very liposoluble booked with the anaesthesia of short, average and long life, Analgesia postoperative In epidural anaesthesia (only or associated with a local anaesthetic) or associated with nerve sedatives: neurolept – analgesia.

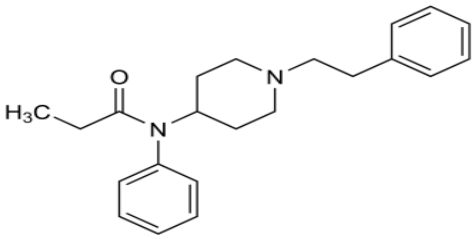

Figure 9. Chemical structure of Fentanyl.

- Pethidine: The structural analogy with Morphine and Atropine confers on this drug a double activity analgesic and spasmolytic of atropinic type intended for the treatment of the pains with spasms, or in premedication during the anesthesia.

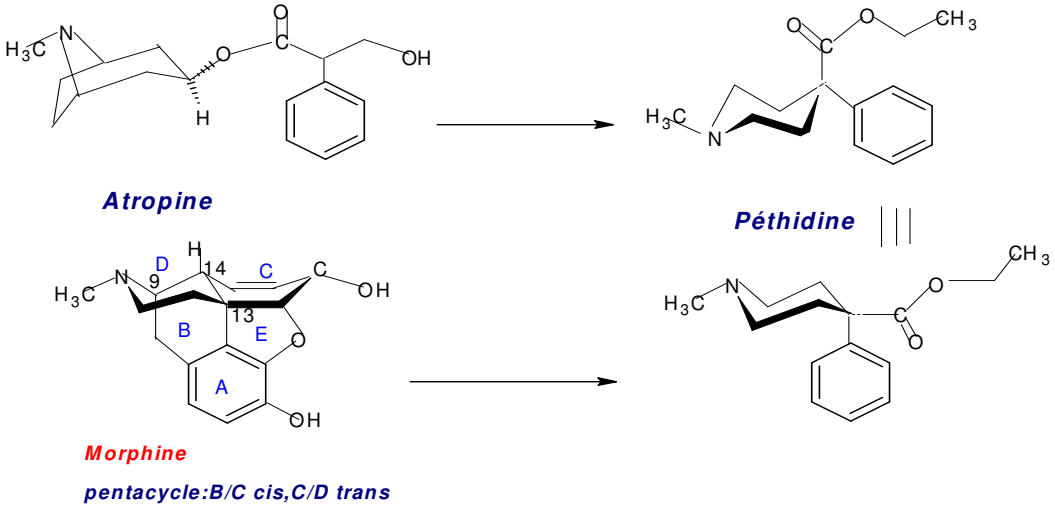

Figure 10. Structural analogy between Péthidine, Morphine and Atropine.

Conclusion

World Health Organization (WHO) proposes a scale of ranking of these drugs comprising three levels (three stages I, II, III), it recommends the methods of use of various categories of analgesics according to the intensity of the pain: Not opiated analgesics, such as paracetamol or Aspirine are advised in the event of pain of low intensity, when the pain is more intense and in the event of inefficiency of the previous products, the weak opiates such as codeine, the tramadol and the dextropropoxyphene, associated or not with paracetamol or Aspirine, are recommended, the morphine ones (Morphine, Pethidine, Fentanyl,…) are advised in the event of very intense pain, however; in the treatment of the acute pains and short time, a strong analgesics can be used from the start.

Taking into account the properties pharmacological (agonists/antagonistic) clean of Buprénorphine, Pentazocine and Nalbuphine, these derivatives should not be associated with analgesics pure agonists such as Morphine. Finaly, the pains of origin neurogene, not very sensitive to opiates and peripheral analgesics can be treated using the antidepressants tricyclic, the alpha2-adrenergic agonists and unquestionable anaesthetic local.

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