

## ENCYCLOPEDIA REVIEW ON ANALGESICS AND IT'S SIDE EFFECTS

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### ABSTRACT

Analgesics are the medications to relieve pain. by reducing inflammation pain is a multifaceted experience that combines physiological and psychological responses to noxious stimuli. It can range from a sharp stab to a dull ache, and may manifest throbbing, pinching, Stinging, burning or sore sensation. The International association for the study of pain defines pain as "an" unpleasant sensory and emotional Experience. associated with resembling that associated with actual or potential tissue damage while acute pain often severe as an alarm system. chronic pain. can significantly impact daily life, affecting function, sleep, and emotional well-being. The choice of pain relief depends upon pain severity. For mild pain, consider acetaminophen or NSAIDs. for Moderate pain includes mild opioids like Tramadol, codeine care severe pain may require strong opioids like Morphine, oxycodone etc.

**KEYWORDS:** Analgesics. NSAIDs, opioids pain, paracetamol Aspirin, Diclofenac.

### INTRODUCTION

Pain is a complex and uniquely personal experience, involving various physiological and perceptual pathways and factors.<sup>[1]</sup> Pain is also known as "an unpleasant sensory and emotional experience associated with actual tissue damage."<sup>[2]</sup> Acute pain is usually self-limiting and serves a protective function, influencing behaviour to avoid further tissue damage and limiting movement to support healing. Chronic pain is defined as pain that persists beyond the normal time expected for tissue healing (usually accepted as 3 months) and without apparent benefit.<sup>[3]</sup>

Chronic pain associated with specific disorders such as cancer, osteoarthritis fibromyalgia or neuropathic pain, often there is no obvious cause for pain that persists despite treatment. Pain serves as a crucial connection between primary diseases and secondary outcomes. It can provoke a dynamic and detrimental interplay among biological, social and psychological factors, leading to disability and poor prognosis in patients. Pain-related psychiatric disorders, such as insomnia, depression, anxiety and impaired social interaction, can exacerbate the progression of primary diseases.<sup>[4]</sup>

Analgesic drugs are the pillar to acute and chronic pain management. Despite their short-term effectiveness, significant concerns regarding drug dependence, addiction and other side effects have been raised.

### Classification of analgesics

The substance Analgesics are that reduces the pain without triggering any mental confusion, paralysis, or any other disturbance to the nervous system.

### Various types of analgesics

1. Simple, Non-Opioid Analgesics: These include drugs like paracetamol (acetaminophen), which is commonly used for mild to moderate pain and fever.
2. Compound Analgesics: These are combinations of different analgesic agents. For example, some medications contain both paracetamol and codeine.
3. Opioid Analgesics (Narcotics): These powerful pain relievers include and overdose.<sup>[5]</sup>

### Examples of analgesics

Below are some examples of the different types of analgesia.

Simple, non-opioid analgesics

Simple, non-opioid analgesics are mostly using analgesics. This group contain acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) such as:

- ibuprofen
- aspirin
- naproxen
- naproxen sodium
- naproxen/esomeprazole
- diclofenac

- etodolac
- indomethacin
- nabumetone
- oxaprozin

**Compound analgesics**

Compound analgesics are medications including a non-opioid along with an opioid, such as low strength codeine.

Examples include:

- co-codamol
- co-codaprin
- co-dydramol

**Opioid analgesics**

Opioid analgesics can be natural or synthetic. These are the strongest type of analgesics. Examples include:<sup>[6]</sup>

- codeine
- fentanyl
- hydrocodone
- meperidine
- methadone
- morphine
- oxycodone
- tramadol

**MECHANISM OF ACTION**

Local tissue injury releases prostaglandins. Prostaglandins have two major actions:

- Sensitize pain receptors and lower the entry for painful stimuli
- Raise the activation of the nerve closing by other inflammatory mediators such as bradykinin, serotonin, and histamine

COX - Cyclooxygenase

Coxib - Selective COX-2 inhibitor

NSAIDs work by suppress the production of prostaglandins by suppressing two types of cyclooxygenase enzymes:

COX-1

- COX-2

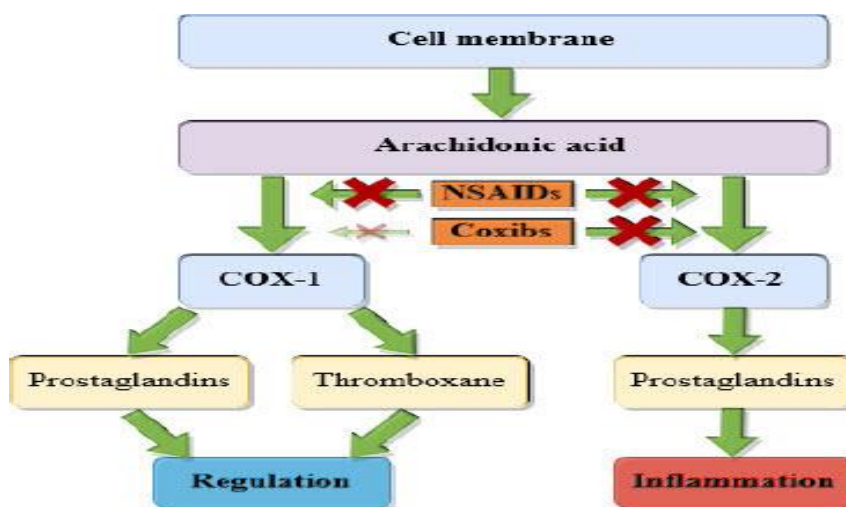
COX-1 is present in all cells, while COX-2 is influencing in the presence of inflammation.

Traditional NSAIDs inhibit both COX enzymes and thus relieve pain, reduce fever and inflammation. Selective COX-2 inhibitors (coxibs) inhibit the COX-2 enzyme primarily and thus exerts anti-inflammatory effects.<sup>[7]</sup>

Acetaminophen, or paracetamol, acts by a different mechanism by inhibiting the COX-3 enzyme in the brain. It produces analgesia by altering the pain perception in the brain but has a little anti-inflammatory effect.<sup>[8]</sup>

**Simple and nonopioid analgesics**

The NSAIDs contains of six heterogenous group of major chemical classes of drugs that are primarily used as anti-inflammatory agents. The main mechanism of action of NSAIDs is reduces the formation of prostaglandins (as well as prostacyclin and thromboxane) from arachidonic acid via inhibition of cyclooxygenase enzymes 1 and 2 (COX-1 and COX-2, also called as prostaglandin synthase), The nomenclature of the COX enzymes is slightly misleading, as the synthase enzyme has both a cyclooxygenase (COX) and a peroxidase (POX) binding site.<sup>[9]</sup>



The COX-1 enzyme is variably expressed in nearly all tissues, and is responsible for synchronizing normal cellular processes. COX-2 is generally invisible in most tissues – except for its native expression in the brain,

kidney, and bone – but is highly activated in states of inflammation, leading to the production of pro-inflammatory prostaglandins. While many processes subscribed to the formation of inflammation, the

prostaglandins are putatively as the primary inflammatory mediators.<sup>[10]</sup> The various downstream effects of prostaglandin synthesis depend on the differential expression of COX-1 and COX-2 enzymes in different tissues at the sites of inflammation.<sup>[11][12]</sup>

### COMPOUND ANALGESICS

Compound analgesics are those with multiple active ingredients; they include many of the stronger prescription analgesics.

Active ingredients that are mostly used in compound analgesics include:

- aspirin or ibuprofen
- caffeine
- codeine or oxycodone
- paracetamol (acetaminophen)
- phenacetin

There is evidence that a compound of two analgesics with different mechanism of action can have an increased painkilling effect over the sum of the effect of each individual analgesic.<sup>[13][14]</sup>

### OPIOID ANALGESICS

Opioids act both pre synaptically and postsynaptically to produce an analgesic effect. Pre synaptically, opioids block calcium channels on nociceptive afferent nerves to inhibit the release of neurotransmitters such as substance P and glutamate, which contribute to nociception. Post synaptic ally, opioids open potassium channels, which hyperpolarize cell membranes, increasing the required action potential to generate nociceptive transmission. The mu, kappa, and delta-opioid receptors mediate analgesia spinally and supra spinally.<sup>[15]</sup>

Some opioid agents can influence serotonin kinetics in the presence of other serotonergic agents. The suggested mechanism for this is through either weak serotonin reuptake inhibition and raises the release of intrasynaptic serotonin through inhibition of gamma-aminobutyric acidergic presynaptic inhibitory neuron on serotonin neurons. These opioids contain tramadol, oxycodone, fentanyl, methadone, dextromethorphan, meperidine, codeine, and buprenorphine. These opioids may possible

to cause serotonin syndrome and should be used cautiously with other agents with serotonergic activity.

Opioids including methadone also have activity at the N-methyl-D-aspartate (NMDA) receptor. Methadone binds to the NMDA receptor and antagonizes the effect of glutamate, which theoretically explains why methadone has efficacy in the treatment of neuropathic pain above other opioids.<sup>[16]</sup>

### SIDE EFFECTS

Most of the analgesics can cause side effects. These may range in severity from mild to severe.<sup>[17][16]</sup>

Less serious side effects may include:

- heartburn
- indigestion
- nausea
- vomiting
- constipation
- diarrhea
- headaches
- dizziness
- drowsiness

More serious possible side effects include:

- light sensitivity
- skin rash
- chest pain
- stomach ulcers
- liver damage
- respiratory depression, which is when breathing is too slow or shallow to meet the body's needs

Opioid analgesics may cause more side effects when compare to simple, non-opioid analgesics. More over feasible side effects includes following:

- additional pain
- inability to concentrate
- itching
- reduced ability to fight infections
- issues with urinating or passing stool
- erectile dysfunction
- reduced fertility
- difficulty breathing

### DOSES OF ANALGESICS

DRUG	DOSES	DOSAGE FORMS
ACETAMINOPHEN	Adult dose:650-1000mg 4-6hrs Childdose: 15mg/kg every 6hrs up to 60mg/kg/day	Tablet, capsule, syrup, oral solution, suspension, rectal suppository or intravenous
NSAIDS: there are different types of NSAIDS are available such as 1. ASPIRIN	325-650mg every 4-6hrs Maximum dose:4000mg/day	Tablet, capsule, rectal suppository
2. IBUPROFEN	400mg every 4-6hrs Maximumdose:3200mg(acute) 2400mg(chronic)	Tablet, capsule, suspension, intravenous
3. DICLOFENAC	50mg every 8hrs	Tablet, capsule, intravenous, topical (creams,

	Maximum dose:150mg	gels, ointment) or ophthalmic administration
4. INDOMETHACIN	Immediate release:25-50mg every 8-12hrs Control release:75mg once or twice daily Maximum dose:150mg	Capsule, suspension, intravenous, or rectal suppository.
5. MELOXICAM	7.5-15mg once daily Maximum dose:15mg	Tablet, capsule, suspension, intravenous.
6. NAPROXEN	250-500mg every 12hrs 275-550mg every 12hrs Maximum dose:1250mg	Tablet, capsule, suspension,
7. CELECOXIB	200mg daily, 100mg every 12hrs Maximum dose:400mg/day	capsule

## DRUG INTERACTIONS

**1. Drug combinations:** Aspirin and NSAIDs or multiple NSAIDs

**Effect:** Increased risk of serious GI complications. Risk increases with increased dose and number of agents.

**Management:** Avoid concurrent use of more than one NSAID, if possible. Consider adding gastroprotective agents.

**2. Drug combinations:** Anticoagulants and NSAIDs

**Effect:** Increased risk of bleeding (especially GI) and increased oral warfarin activity.

**Management:** Avoid concurrent use of NSAID; monitor prothrombin time and occult blood in urine and stool.

**3. Drug combinations:** Corticosteroids and NSAIDs

**Effect:** Increased GI side effects, including ulceration and haemorrhage.

**Management:** Avoid concurrent use of NSAID and consider adding a gastroprotective agent.

**4. Drug combinations:** SSRIs and NSAIDs

**Effect:** Increased risk of GI bleeding

**Management:** Avoid concurrent use of NSAID

**5. Drug combinations:** Aspirin and ibuprofen or naproxen.

**Effect:** Reduced antiplatelet effects of aspirin.

**Management:** Not seen with other NSAIDs or acetaminophen.

**6. Drug combinations:** Antihypertensive agents and NSAIDs.

**Effect:** Use of NSAIDs may increase blood pressure.

**Management:** Monitor blood pressure and cardiac function.

**7. Drug combinations:** Antidiabetic agents (eg, sulfonylureas) and aspirin.

**Effect:** Increased hypoglycaemics effect.

**Management:** Avoid concurrent use and monitor blood glucose concentration.

**8. Drug combinations:** Lithium and NSAIDs

**Effect:** Increased steady-state lithium concentration and lithium toxicity.

**Management:** Monitor lithium concentrations. Interactions are less likely with aspirin than with naproxen or ibuprofen.

**9. Drug combinations:** Methotrexate and NSAIDs

**Effect:** Reduced renal clearance. Increased plasma methotrexate concentration.

**Management:** Avoid NSAIDs with high-dose methotrexate.

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## CONCLUSION

In this article we have enlightened about Analgesic drugs which are currently in use are either narcotics or non-narcotics which have proven side and toxic effects like liver toxicity, kidney damage and heart problems. Opioid pain relief can cause constipation and other digestive problems as they reduce nervous system activity. Mixing opioids with other medication or alcohol leads to toxicity. Heroin and opium are also opioids that are illegal and which people use recreationally. An overdose can be fatal any one experiencing an opioid overdose will need immediate medical attention.

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