

Paracetamol (Acetaminophen) and other NSAIDs

- It does not possess anti-inflammatory activity because it is ineffective in the presence of peroxides at inflammatory site.
- It produces very little GI toxicity and can be administered in patients intolerant to other NSAIDs.
- It is metabolized to N-acetyl para-amino-benzo quinoneimine (NAPQ) by microsomal enzymes. This metabolite has high affinity for -SH groups and can result in hepatotoxicity. Normally acetaminophen is a safe drug because glutathione produced by the liver combines with NAPQ to detoxify it. However chronic alcoholics are predisposed to toxicity because: Glutathione production decreases due to liver disease.
- Alcohol is a powerful inducer of microsomal enzymes. It increases the production of NAPQ from acetaminophen resulting in toxicity
- Acetaminophen toxicity can be decreased by providing sulfhydryl donors like N-acetylcysteine (antidote of choice)

Other Non-selective COX Inhibitors

- **Indomethacin** possesses immunosuppressive properties apart from its COX inhibitory action. It causes more GI upset than other NSAIDs. It is implicated in causing headache (analgesic causing pain) and sedation.
- **Phenylbutazone** causes agranulocytosis due to bone marrow suppression.
- **Propionic acid derivatives include ibuprofen, ketoprofen and flurbiprofen.** Ketoprofen possesses additional lysosomal stabilizing action and flurbiprofen can be used topically as eye drops. Ibuprofen has been cleared for paediatric patients.
- **Naproxen and oxaprozin** are long acting drugs that also inhibit leucocyte migration.
- **Mefenamic acid** also possesses PG receptor antagonistic activity. It is very useful in dysmenorrhoea.
- **Phenacetin** (prodrug of paracetamol) is implicated in causing analgesic nephropathy
- **Ketorolac** is the only NSAID that can be used i.v. It is also available as eye drops. Course longer than 5 days is not recommended.
- **Piroxicam and tenoxicam** are longest acting NSAIDs due to enterohepatic cycling. Oxaprozin is another very long acting NSAID.
- **Apazone** possess potent uricosuric activity. It is indicated in conditions, in which other NSAIDs have failed