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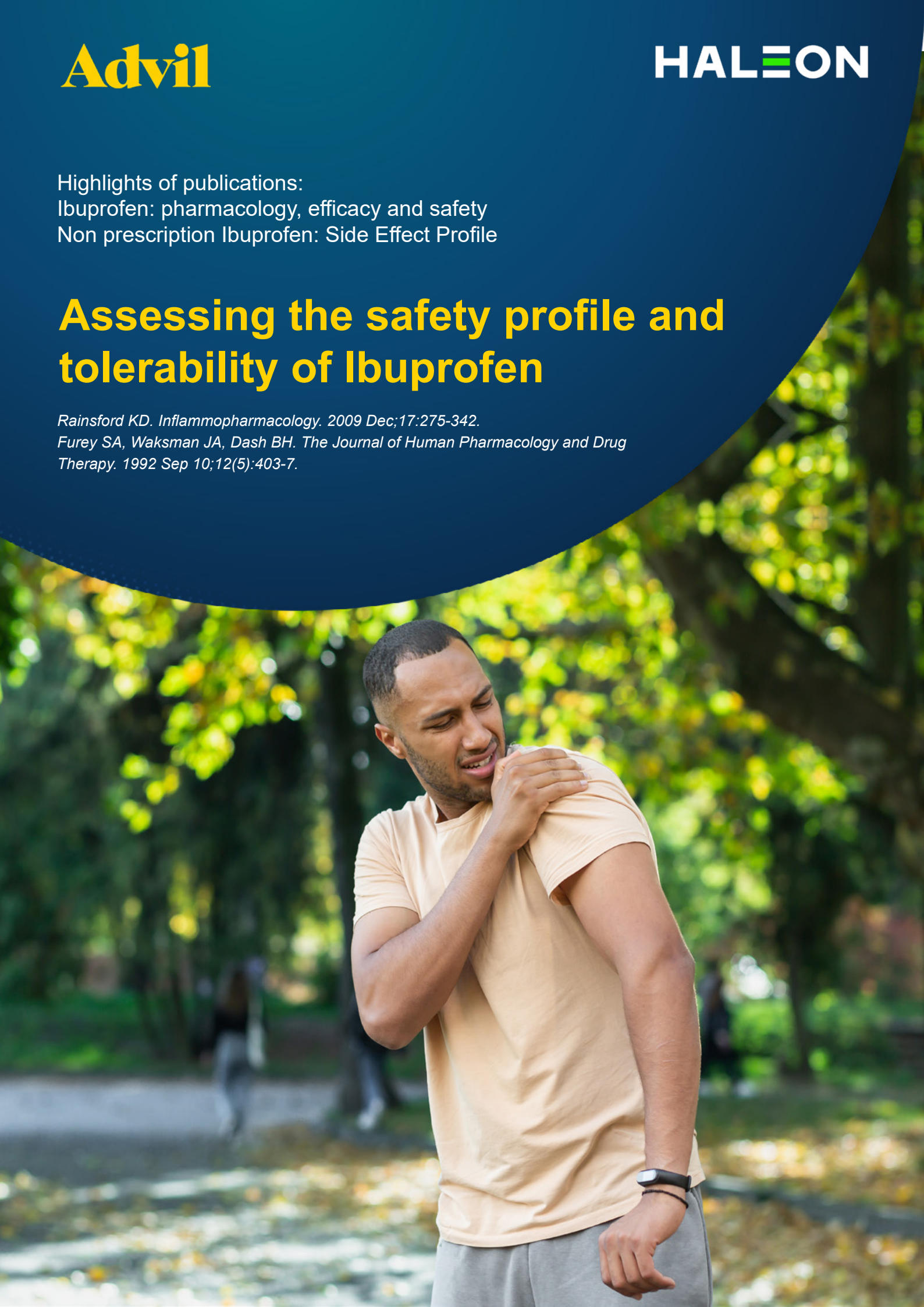
Highlights of publications:
Ibuprofen: pharmacology, efficacy and safety
Non prescription Ibuprofen: Side Effect Profile

Assessing the safety profile and tolerability of Ibuprofen

Rainsford KD. Inflammopharmacology. 2009 Dec;17:275-342.
Furey SA, Waksman JA, Dash BH. The Journal of Human Pharmacology and Drug Therapy. 1992 Sep 10;12(5):403-7.

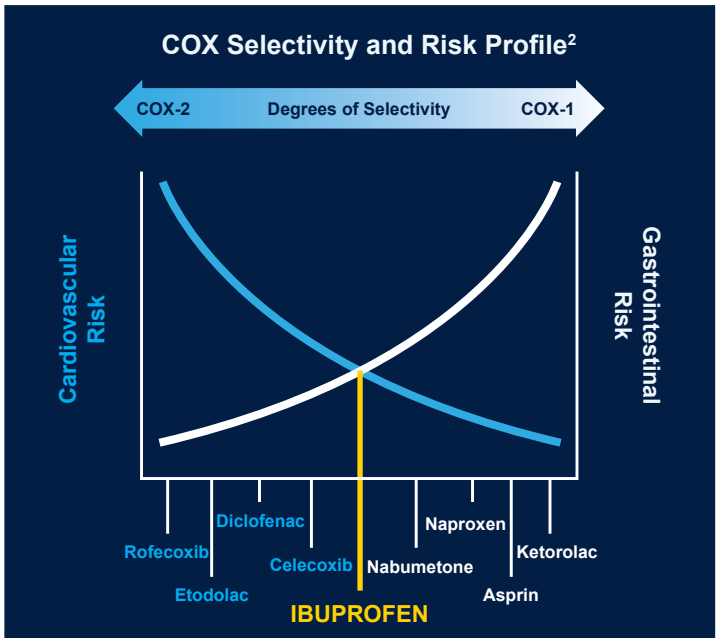


Background

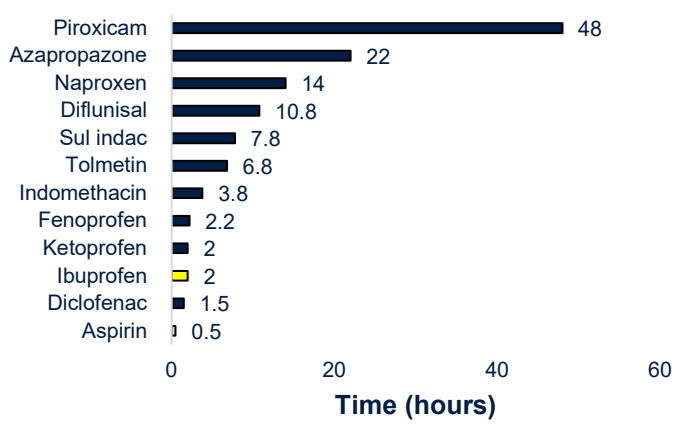
- Ibuprofen is clinically proven to provide relief for a variety of pain conditions and indicated for the temporary relief of minor aches and pains due to headache, toothache, backache, menstrual cramps, common cold, muscular aches, minor pain of arthritis and temporary reduction of fever
- As an analgesic-antipyretic-anti-inflammatory drug, ibuprofen ranks below aspirin and acetaminophen in non-prescription OTC use. It has low risk for tolerability issues among these three and rarely causes serious adverse reactions or accidental ingestion-related deaths[1]
- Use suggests no significant difference in gastrointestinal event rates in clinical studies between ibuprofen and acetaminophen at OTC strength[1]
- OTC ibuprofen is widely regarded as safe with low risks, supported by regulatory and clinical guidelines worldwide[1]

Balanced COX inhibition and short half-life: Key factors in Ibuprofen proven safety profile

Pharmacodynamics[2]



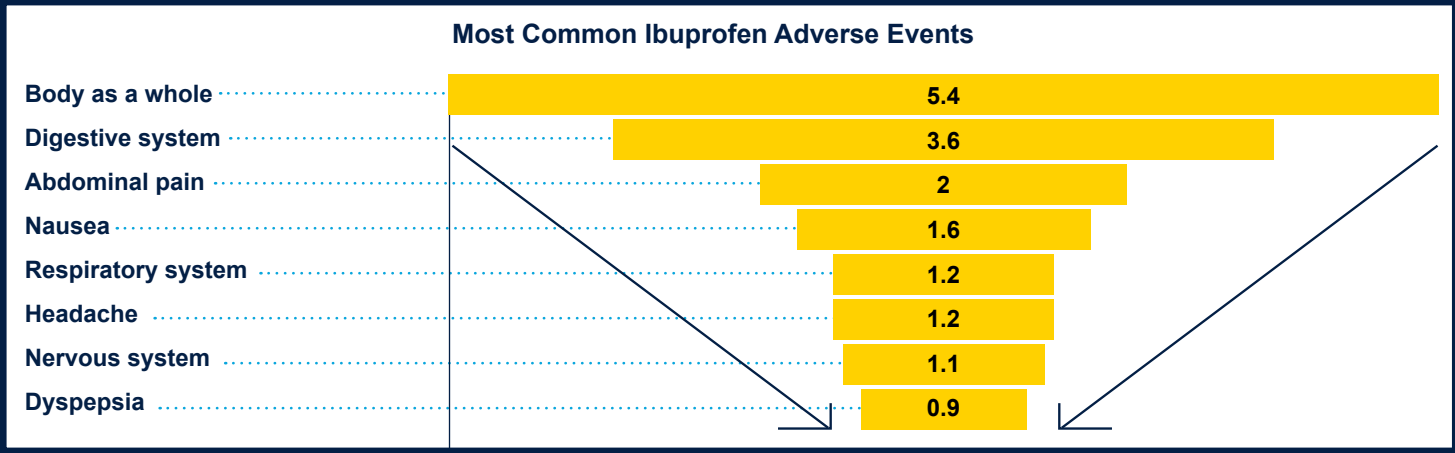
Pharmacokinetics[3]



- Ibuprofen has a short plasma half-life, leading to rapid metabolism and reduced systemic exposure
- Lack of pathologically-related metabolites

- Moderate inhibition of both COX-1 and COX-2, as shown by the mean residence time of the drug in the body may account for the low GI, CV and renal risks from ibuprofen, especially at OTC doses
- Ibuprofen's short plasma half-life and lack of pathologically-related metabolites also contribute to its low risk for tolerability issues

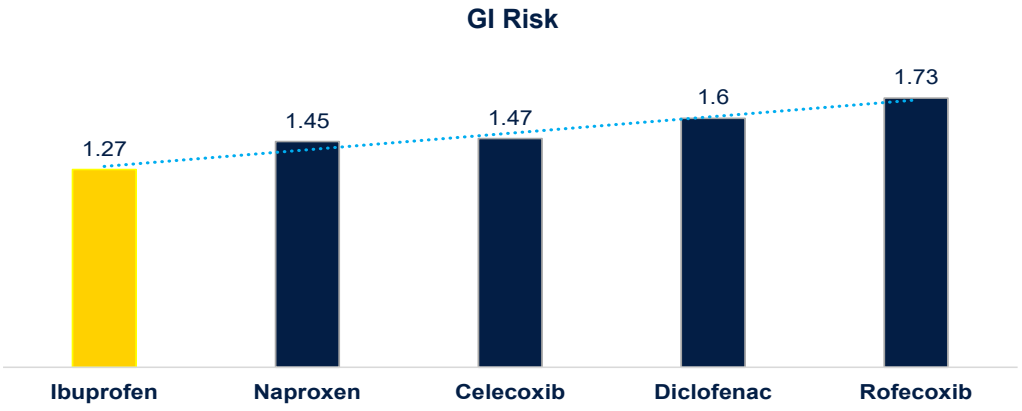
Percentage of most frequent significant adverse events associated with Ibuprofen[4]



Gastrointestinal (GI) safety profile

Studies indicate that ibuprofen is generally well-tolerated in terms of GI effects when used at over-the-counter (OTC) doses of up to 1200 mg per day

- GI symptoms (nausea, epigastric or abdominal pain, dyspepsia, diarrhea, flatulence, GI bleed and constipation) are among more frequent reactions observed with OTC use of ibuprofen and generally the symptoms are of the same order as in subjects who have received placebo
- GI events are comparatively less severe with comparison to other NSAIDs such as coxibs and diclofenac

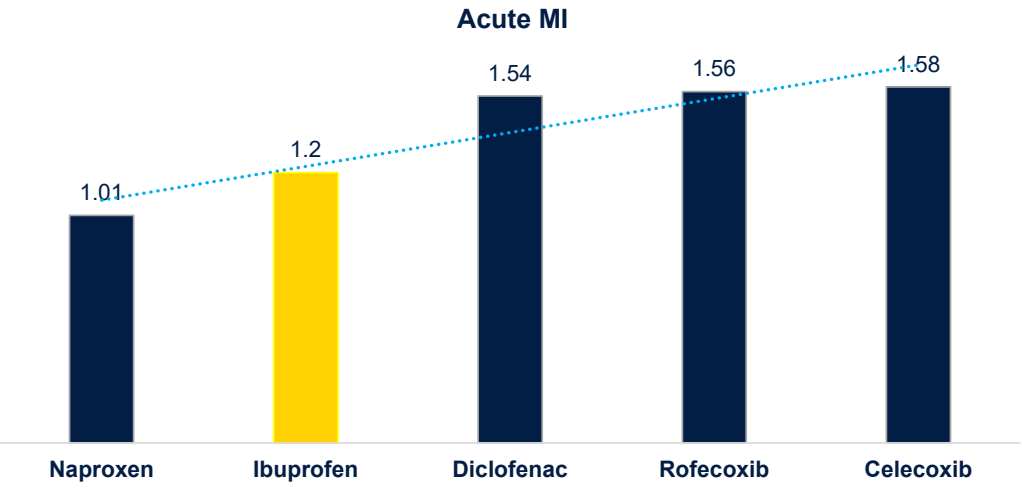


The unadjusted 180-day risk of GI complications per 100 users ranged from 1.27 (ibuprofen) to 1.73 (rofecoxib) and, due to confounding, made the coxibs appear more gastrotoxic than most nonselective NSAIDs[5]

Cardiovascular (CV) safety profile

Research suggests that ibuprofen has a relatively low to moderate risk of being associated with serious cardiovascular conditions, including myocardial infarction (MI)

- OTC ibuprofen poses no greater risk of acute MI compared to other NSAIDs, or placebo
- In a case-control study, OTC ibuprofen had similar cardiovascular risks to OTC naproxen



The unadjusted 180-day risk of acute MI per 100 users ranged from MI was 1.01 with naproxen, 1.20 with ibuprofen, compared with 1.54 with diclofenac, 1.56 with rofecoxib and 1.58 with celecoxib[5]

Data shows that combined risks of serious CV and GI events with ibuprofen are relatively low as compared to other NSAIDs, particularly in the more severe category

Other safety profile related to Ibuprofen

Hepatic safety[1]

- Ibuprofen at OTC doses is not observed to pose a risk for liver injury
- Available data suggest that hepatic reactions with ibuprofen are likely rare, as there are no specific reports of liver reactions from OTC use in trials. Therefore, hepatotoxicity is unlikely to be a significant risk factor at OTC dosages with ibuprofen

Renal safety[1]

- Low probability of renal events with OTC use of ibuprofen
- Clinical data show that taking Ibuprofen as directed at OTC dosing for less than 10 days is associated with a low risk of kidney-related side effects
- Ibuprofen is a low-risk factor for developing acute or chronic renal conditions when used as directed

Ibuprofen

Cutaneous reactions[1]

- Serious adverse drug reactions (ADRs) in the skin are rare
- Other side effects (thrombocytopenia, agranulocytosis, anemia, aseptic meningitis and anaphylactoid reactions) are rare at OTC dose

Central nervous system (CNS) safety[6]

- The occurrence of CNS symptoms associated with ibuprofen and acetaminophen was comparable to that observed with placebo
- The likelihood of experiencing typical CNS effects, such as drowsiness and dizziness, is considerably minimum at the OTC dose

Conclusion

- Ibuprofen at OTC doses has a favorable safety profile when used as directed, which can be altered by increasing dose and duration of use, use with some concomitant medications, and among patient populations with added risks. At OTC doses, it has a comparatively low incidence of serious GI events and minimal risk of causing renal and associated cardiovascular events. Furthermore, it is not observed to pose a risk for developing liver injury.
- The pharmacodynamic and pharmacokinetic properties of ibuprofen support its low risk for tolerability issues. These properties include its moderate inhibition of COX-1 and COX-2, a short plasma half-life of elimination, minimal development of pathologically related metabolites, and low residence time in the body

Ibuprofen is a well-tolerated and effective medication for various types of pain associated with acute or chronic inflammatory conditions in both adults and children when used as directed. It has been shown to cause minimal side effects related to serious gastrointestinal events in clinical studies and only a limited risk of causing renal and cardiovascular issues

References

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5. Schneeweiss, S., Solomon, D. H., Wang, P. S., Rassen, J., & Brookhart, M. A. (2006). Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 54(11), 3390-3398
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