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CLINICAL PHARMACOLOGY OF FLURBIPROFEN

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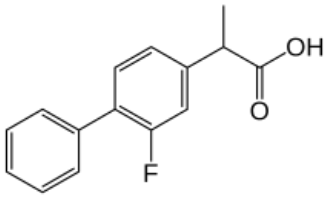
ABSTRACT

Flurbiprofen is a propionic acid derivative and is a nonselective cyclooxygenase inhibitor. Flurbiprofen is approved for the symptomatic treatment of rheumatoid arthritis, juvenile arthritis, pain, ankylosing spondylitis, acute gout arthritis, bursitis, postoperative dental pain, and primary dysmenorrhoea. In adults, the dose of flurbiprofen in 40 mg once-daily or twice-daily. Flurbiprofen is hydroxylated into 4'-hydroxy flurbiprofen by CYP2C9 and is conjugated with glucuronic acid by different glucuronosyl transferases and UGT2B7 catalyses the glucuronidation of flurbiprofen at the highest activity. The pharmacokinetics of flurbiprofen have been studied in CYP2C9 extensive and poor metabolizers and the elimination half-life of flurbiprofen is 5.1±0.3 and 6.1±0.6 hours (P-value = 0.0004) in extensive and poor metabolisers, respectively. The efficacy and safely of flurbiprofen, the prophylaxis with flurbiprofen, the treatment of patients with flurbiprofen, and the trials conducted with flurbiprofen have been reviewed. The concentration of flurbiprofen in different human tissues has been reviewed following topical and oral administration and the concentration of flurbiprofen in fat, tendon, periosteum, and muscle is higher following the topical than oral administration. The interaction of flurbiprofen with drugs and the toxicity induced by flurbiprofen have been reviewed. The aim of this study is to review the efficacy and safely of flurbiprofen, the prophylaxis with flurbiprofen, the treatment of patients with flurbiprofen, and the trials conducted with flurbiprofen. In addition, the metabolism of flurbiprofen, the tissue concentration of flurbiprofen, the interaction of flurbiprofen with drugs, and the toxicity induced by flurbiprofen have also been reviewed.

KEYWORDS: Drug-interaction, efficacy-safely, flurbiprofen, metabolism, pharmacokinetics, prophylaxis, tissue-concertation, toxicity, and trials.

INTRODUCTION

Flurbiprofen is a propionic acid derivative. Flurbiprofen is a nonselective cyclooxygenase inhibitor with the effects and adverse-effects common to the non-steroidal anti-inflammatory drugs. Flurbiprofen has inhibitory effects on leukocyte function. Flurbiprofen is approved for use in the symptomatic treatment of rheumatoid arthritis, juvenile arthritis, pain, ankylosing spondylitis, acute gout arthritis, tendinitis, bursitis, headache, postoperative dental pain, and primary dysmenorrhoea. Flurbiprofen is comparable in efficacy to aspirin for the control of the signs and symptoms of rheumatoid arthritis and osteoarthritis and in adults the dose of flurbiprofen is 40 mg once-daily or twice-daily. Flurbiprofen is hydroxylated into 4'-hydroxy flurbiprofen by CYP2C9 and is conjugated with glucuronic acid by different glucuronosyl transferases and UGT2B7 possesses the highest activity in the glucuronidation of flurbiprofen. The pharmacokinetics of flurbiprofen have been studied in CYP2C9 extensive metabolizers and in CYP2C9 poor metabolizers and the elimination half-life of flurbiprofen is 5.1±03 hours in extensive metabolizers and is about 6.1±0.6 hours in poor metabolizers (P-value < 0.0004).[1]



Flurbiprofen molecular structure (molecular weight = 244.265 grams/mole)

Literature search

The literature search was performed electronically using PubMed database as search engine and the following key words were used: "flurbiprofen efficacy, safely", "flurbiprofen prophylaxis", "flurbiprofen treatment", "flurbiprofen trials", "flurbiprofen metabolism", "flurbiprofen tissue concentration", "flurbiprofen pharmacokinetics", "flurbiprofen drug-interaction", and "flurbiprofen toxicity". In addition the book: Goodman@Gilman's. The Pharmacological basis of Therapeutics.[1] has been consulted.

RESULTS

Efficacy and safely of flurbiprofen

Six studies on the efficacy and safely of flurbiprofen have been reported. Flurbiprofen, administered at the daily dose of 80 mg, effectively and safely treated patients with rheumatoid arthritis.[2] Flurbiprofen, administered at the dose of 40 mg twice-daily, effectively and safely relieved pain in patients who underwent surgery.[3] Flurbiprofen penetrates into the human skin in significant amounts and effectively and safely relieved pain in patients undergoing skin surgery.[4] Flurbiprofen was administered at the daily dose 40 mg to 101 patients and at the daily dose of 80 mg to 100 patients. Patients had osteoarthritis and flurbiprofen effectively and safely treated these patients.[5] Flurbiprofen was administered at the daily dose of 40 mg to patients undergoing surgery and flurbiprofen effectively reduced postoperative pain, nausea, and vomiting.[6] Flurbiprofen axetil, administered at the daily dose of 50 mg, effectively relieved pain in patients who underwent surgery and no adverse-effects were reported.[7]

Prophylaxis with flurbiprofen

Three studies on the prophylaxis with flurbiprofen have been reported. Twenty-three patients suffering from migraine received either flurbiprofen at the daily dose 100 mg twice-daily or placebo and flurbiprofen prevented migraine more effectively (P-value < 0.05) than placebo.[8] Topic 0.03% flurbiprofen and 1% indomethacin was administered to patients with pseudophakic cystoid macular oedema and flurbiprofen prevented cystoid macular oedema more effectively (P-value < 0.05) than indomethacin.[9] Fifty-two patients undergoing extracapsular cataract extraction with lens implantation received either topic flurbiprofen or diclofenac or placebo. The change in pupil size was significantly higher in treated patients. Pre-operative flurbiprofen or diclofenac maintains intraoperative mydriasis more effectively than placebo.[10]

Treatment of patients with flurbiprofen

Eight studies on the treatment of patients with flurbiprofen have been reported. Flurbiprofen, administered locally at the dose of 8.75 mg to 17 patients with acute pharyngitis, offers a useful first-line treatment option for symptomatic relief of patients with acute pharyngitis.[11] Flurbiprofen, administered at the daily dose to 50 mg to 34 patients undergoing thoracoscopic surgery, attenuated the postoperative pain.[12] Treatment with flurbiprofen 0.03% solution administered topically to eyes is an effective treatment for corneal neovascularization induced by contact lenses.[13] Flurbiprofen, administered at the daily dose of 40 mg, is a potential treatment of Alzheimer's disease.[14] Flurbiprofen, administered at the dose of 40 mg twice-daily for 14 days, is an effective treatment of patients with soft-tissue lesions.[15] Flurbiprofen, administered at the daily dose of 75 to 400 mg, is an effective treatment of patients with degenerative and inflammatory arthritis.[16] Eleven patients (8 patients had rheumatoid arthritis and 3 patients had osteoarthrosis), received flurbiprofen at the daily dose of 150 mg and this treatment effectively treated the patients.[17] Flurbiprofen was administered at the daily dose of 75 to 250 mg to 828 patients with arthritis. Flurbiprofen is an effective anti-inflammatory analgesic agent which is well-tolerated by the majority of patients and only 13% of patient withdrawn from the study because of the adverse-effects.[18]

Trials conducted with flurbiprofen

Six studies on the trials conducted with flurbiprofen have been reported. An open-label, non-inferiority, randomized, controlled trial was conducted in 250 patients, aged 62.8±10.5 years, with osteoarthritis of the knee who received either flurbiprofen cataplasms or loxoprofen sodium cataplasms and both drugs were administered for 28 days. The decline of intense pain was superior (P-value < 0.001) in patients who received flurbiprofen cataplasms. These results indicate that flurbiprofen cataplasm is superior to loxoprofen sodium cataplasm for treatment of patients with osteoarthritis of the knee.[19] A multicentre, randomized, active-controlled, open-label, non-inferiority, phase III trial was conducted in 311 patients with osteoarthritis of the knee who received either S-flurbiprofen plaster or diclofenac gel and both drugs were administered for 2 weeks. The clinical symptom was the relief of pain in the walking and the adverse-effects occurred in 5.8% of patients who received S-flurbiprofen plaster and diclofenac gel. S-flurbiprofen plaster was non inferior to diclofenac gel in treatment of pain in patients with osteoarthritis of the knee.[20] A phase II, randomized, double-blind, placebo-controlled, dose-finding trial was conducted in 509 patients with osteoarthritis of the knee who received S-flurbiprofen plaster at 10, 20, or 40 mg applied to the knee once-daily for 2 weeks. The primary endpoint was the relief of knee pain. Pain relief was observed with all doses of S-flurbiprofen plaster and the 40 mg of S-flurbiprofen plaster showed remarkable pain relief and was the optimal tested dose.[21] A randomized, controlled trial was conducted with flurbiprofen axetil in patients undergoing surgery. Patients treated with flurbiprofen axetil had lower pain (P-value < 0.01) than untreated patients. Preoperative use of flurbiprofen axetil resulted in significantly lower postoperative pain scores, but nausea, vomiting, and opioid consumption were similar in treated and untreated patients.[22] A randomized, controlled trial was conducted in patients with moderate-to-severe sore throat who received either flurbiprofen administered at the daily dose of 8.75 mg (N = 101) or lozenges administered at the daily dose of 9 mg daily (N = 97). Reductions in pain, difficulty in swallowing, and throat swelling were lower (P-value < 0.05) in patients who received flurbiprofen. Flurbiprofen and lozenges were effective and well-tolerated treatment of sore throat pain.[23] A prospective, randomized, placebo-controlled trial was conducted in 100 patients undergoing post-endoscopic retrograde cholangiopancreatography

pancreatitis. Forty-seven patients (47.0%) received flurbiprofen axetil at the daily dose of 50 mg and 53 patients (53.0%) received placebo. Pancreatitis occurred in 4.3% of treated patients and in 17.0% of patients who received placebo (P-value < 0.05). Low-dose of flurbiprofen axetil reduced pancreatitis in patients undergoing post-endoscopic retrograde cholangiopancreatography pancreatitis.[24]

Metabolism of flurbiprofen in human liver

Two studies on the metabolism of flurbiprofen have been reported. Tracy et al.[25] observed that the major oxidative metabolite of flurbiprofen is the 4'-hydroxy metabolite which is formed by the cytochrome P450 CYP2C9. Mano et al.[26] stated that flurbiprofen is conjugated with glucuronic acid by UGT1A1, 1A3, 1A9, 2B4, and by UGT2B7 and UGT2B7 catalyses the glucuronidation of flurbiprofen at the highest activity.

Concentration of flurbiprofen in human tissues

Two studies on the concentration of flurbiprofen in human tissues have been reported. Kai et al.[27] measured the concentration of flurbiprofen in human soft-tissues and administered flurbiprofen orally, at the dose of 40 mg twice-daily, to 7 patients, aged 31±13 years, with a body-weight of 64±7 kg, and with a body-mass-index of 23±3 kg/m^2. These authors also administered flurbiprofen topically, at the dose of 20 mg twice-daily, to 9 patients, aged 29±14 years, with a body-weight of 64±8 kg, and with a body-mass-index of 23±3 kg/m^2. Table 1 summarizes the concentration of flurbiprofen is different soft-tissues.

Table 1: Concentration of flurbiprofen in human fat, tendon, muscle, and periosteum. Flurbiprofen was administered orally at the daily dose of 40 mg twice-daily to 7 patients and topically at the dose of 20 mg twice-daily to 9 patients. Values are the mean±SD and the 95% confidence interval, by Kai et al.[27]

Group		Fat (ng/gram)	Tendon (ng/gram)	Muscle (ng/gram)	Periosteum (ng/gram)
Oral	Mean±SD	150±72	186±74	82±36	221±93
N =7	95% CI	84-217	118-254	49-116	135-307
Topical	Mean±SD	992±664	944±602	492±317	455±392
N = 9	95% CI	482-1503	481-1407	248-735	153-756
Comparison	NS	*P-value = 0.0009	*P-value = 0.0018	*P-value = 0.026	*P-value = 0.0012

95% CI = 95% confidence interval. *Mann-Whitney U-test.

This table shows that the tissue concentration of flurbiprofen is higher following topical than oral administration. Flurbiprofen reaches higher concentration in fat, tendon, and periosteum than in muscle. In addition, there is a remarkable variability in the concentration of flurbiprofen in tissues and this variability is accounted by the vide variation in the vital date of subjects included in the study. Turner et al.[28] measured the concentration of flurbiprofen in the cadaveric human pharynx following the administration of 8.75 mg of flurbiprofen lozenge and spry formulations. The concentration of flurbiprofen in the human pharynx was 3.8±0.9 µg following the administration of the lozenge formulation and was 41.5±19.1 µg following the administration of the spry formulation. These results indicate that the concentration of flurbiprofen in the human pharynx is higher following the administration of the spry.

Pharmacokinetics of flurbiprofen

Shin et al.[29] studied the pharmacokinetics of flurbiprofen in 16 healthy volunteers according to CYP2C9 genotype. Ten volunteers were extensive metabolizers and had the genotype CYP2C9*1/*1 and 6 volunteers were poor metabolizers and had the genotype CYP2C9*1/*3. A single oral dose of 40 mg of flurbiprofen was administered to all volunteers. Flurbiprofen is metabolized into 4'-hydroxy flurbiprofen and table 2 summarizes the pharmacokinetic parameters of flurbiprofen is 10 extensive metabolizers and in 6 poor metabolizers.

Table 2: Pharmacokinetic parameters of flurbiprofen which have been obtained in 10 CYP2C9 extensive metabolizers and in 6 CYP2C9 poor metabolizers. Values are the mean±SD, by Shin et al.[29]

Parameter	CYP2C9 extensive metabolizers (N = 10)	CYP2C9 poor metabolizers (N = 6)	*P-value
Peak conc. (µg/ml)	6.4±1.3	6.8±1.8	NS
Tmax (h)	1.6±1.0	1.8±0.9	NS
$T_{1/2}$ (h)	5.1±0.3	6.1±0.6	0.0004
TBC/F (L/h)	1.6±02	1.1±0.1	< 0.0001
$AUC_{0\text{-}24h}$ (µg*h/ml)	25.2±2.6	34.5±2.2	< 0.0001
$AUC_{0\text{-}\infty}$ (µg*h/ml)	26.0±2.7	36.6±2.2	< 0.0001

Tmax = time to reach the peak concentration. $T_{1/2}$ = elimination half-life. TBC = total body clearance. F = bioavailability. AUC = area under the concentration-time curve. *One-way ANOVA.

This table shows that flurbiprofen is rapidly absorbed as the time to reach the peak concentration is about 1 hour. Flurbiprofen is slowly eliminated as the elimination half-life is 5.1 hours in extensive metabolizers and is 6.1

hours in poor metabolizers thus extensive metabolizers eliminate flurbiprofen more rapidly than poor metabolizers. The total body clearance of flurbiprofen is 1.6 L/h in extensive metabolizers and is 1.1 L/h in poor metabolizers and the area under the concentration-time curve of flurbiprofen is lower in extensive than in poor metabolizers.

Interaction of flurbiprofen with drugs

Four studies on the interaction of flurbiprofen with drugs have been reported. Omeprazole is an inhibitor of CYP2C9 thus omeprazole reduces the elimination half-life of flurbiprofen.[30] Brewed tea, grape juice, and cranberry juice are inhibitors of CYP2C9 and the formation-rate of 4'-hydroxy flurbiprofen was reduced to 11±8% by brewed tea, to 10±7% by grape juice, and to 56±16% by cranberry juice. Thus the clearance of flurbiprofen was reduced by brewed tea, grape juice, and by cranberry juice.[31] Maroof et al.[32] observed that flurbiprofen interacts with quinolone antacids, acetaminophen, fluconazole, dapsone and insulin and flurbiprofen increases the toxicity of warfarin, lithium, methotrexate, and cyclosporine. Lei et al.[33] observed that flurbiprofen axetil has a synergistic analgesic effect on sufentanyl thus flurbiprofen axetil reduced the amount of sufentanyl required to achieve satisfactory analgesia.

Toxicity induced by flurbiprofen

Flurbiprofen is a safe drug and only limited information is available about the toxicity induced by flurbiprofen. An 84-year-old man underwent an extracapsular cataract extraction in the left eye. One hour and 30 minutes before surgery, one drop of 0.03% flurbiprofen sodium was instilled into the left eye and flurbiprofen caused intraoperative haemorrhage.[34] A 32-year-old woman was admitted to the hospital approximately 1 hour after taking 20 pieces of 100 mg of flurbiprofen to commit a suicide and flurbiprofen caused nausea and vomiting symptoms. The patient underwent gastric lavage and carbon was administered through a nasogastric probe and the patient recovered uneventfully and was discharged with the recommendation to have a psychiatric visit.[35]

DISCUSSION

Flurbiprofen is a propionic acid derivative and is a nonselective cyclooxygenase inhibitor. Flurbiprofen is approved for treatment of rheumatoid arthritis, juvenile arthritis, pain, ankylosing spondylitis, acute gout arthritis, tendinitis, bursitis, headache, postoperative dental pain, and primary dysmenorrhoea. In adults, the dose of flurbiprofen is 40 mg once-daily or twice-daily.[1] The efficacy and safely of flurbiprofen have been reviewed. Flurbiprofen, administered at the daily dose of 80 mg, effectively and safely treats patients with rheumatoid arthritis.[2], flurbiprofen, administered at the dose of 40 mg twice-daily, effectively and safely treats pain in patients who underwent surgery.[3], flurbiprofen penetrates into the human skin in significant amounts and effectively and safely treats pain in patients who underwent skin surgery.[4] flurbiprofen was administered at the daily dose of 40 mg to 101 patients and at the daily dose of 80 mg to 100 patients. Patients had osteoarthritis and flurbiprofen effectively and safely treats the patients.[5] flurbiprofen, administered at the daily dose of 40 mg, effectively reduces postoperative pain, nausea, and vomiting in patients who underwent surgery.[6] and flurbiprofen axetil, administered at the daily dose of 50 mg, effectively reliefs pain in patents who underwent surgery.[7] These results indicate that flurbiprofen effectively and safely treats rheumatoid arthritis and osteoarthritis, flurbiprofen reduces pain, nausea and vomiting in patients undergoing surgery, and flurbiprofen axetil effectively reliefs pain in patients undergoing surgery. The prophylaxis with flurbiprofen has been reviewed. Flurbiprofen, administered at the daily dose of 100 mg twice-daily, prevents migraine more effectively (P-value < 0.05) than placebo.[8] topic 0.03% flurbiprofen prevents pseudophakic cytosol macular oedema more effectively (P-value < 0.05) than 1% indomethacin.[9] patients undergoing extracapsular cataract extraction with lens implantation received either topic flurbiprofen or diclofenac or placebo. The change in pupil size was significantly higher in treated patients. Pre-operative flurbiprofen or diclofenac is effective in maintaining intraoperative mydriasis more effectively than placebo.[10] These results indicate that flurbiprofen prevents migraine, topic flurbiprofen prevents cystoid macular oedema more effectively than indomethacin, and pre-operative flurbiprofen or diclofenac maintains intraoperative mydriasis more effectively than placebo. The treatment of patients with flurbiprofen has been reviewed. Flurbiprofen, administered at the dose of 8.75 mg, treats patients with acute pharyngitis.[11] flurbiprofen, administered at the daily dose of 50 mg, reliefs pain in patients who underwent thoracoscopic surgery.[12] flurbiprofen solution administered topically to eyes effectively treats corneal neovascularization induced by contact lenses.[13] flurbiprofen administered at the daily dose of 40 mg is a potential treatment of Alzheimer's disease.[14] flurbiprofen, administered at the daily dose of 40 mg for 14 days, effectively treats patients with soft-tissue lesions.[15] flurbiprofen, administered at the daily dose of 75 to 100 mg, effectively treats patients with degenerative and inflammatory arthritis.[16] flurbiprofen, administered at the daily dose of 150 mg, effectively treats patients with rheumatoid arthritis or with osteoarthritis.[17] and flurbiprofen, administered at the daily dose of 75 to 250 mg, effectively treats patients with arthritis and flurbiprofen is an effective anti-inflammatory analgesic which is well-tolerated by the majority of patients.[18] These results indicate that flurbiprofen treats acute pharyngitis and postoperative pain, topical flurbiprofen treats corneal neovascularization induced by contact lenses, flurbiprofen is a potential treatment of Alzheimer's disease, flurbiprofen treats patients with soft-tissue lesions, inflammatory arthritis, rheumatoid arthritis, and osteoarthritis, and flurbiprofen is an effective anti-inflammatory analgesic which is well-tolerated in the majority of patients. The trials conducted with

flurbiprofen have been reviewed. An open-label, non-inferiority, randomized, controlled trial was conducted in patients with osteoarthritis of the knee who received either flurbiprofen cataplasm or loxoprofen sodium cataplasm for 28 days. The decline of intense pain was superior (P-value < 0.001) in patients who received flurbiprofen cataplasm.[19] a multicentre, randomized, active-controlled, open-label, non-inferiority, phase III trial was conducted in patients with osteoarthritis of the knee who received either S-flurbiprofen plaster or diclofenac gel and both drugs were administered for two weeks. S-Flurbiprofen plaster is not inferior to diclofenac gel in relieving of pain in the walking and both drugs are well-tolerated.[20] a phase II, randomized, double-blind, placebo-controlled, dose-finding trial was conducted in patients with osteoarthritis of the knee who received S-flurbiprofen plaster at 10, 20, or 40 mg applied to the knee once-daily for two weeks and this treatment reliefs the pain.[21] a randomized, controlled trial was conducted with flurbiprofen axetil in patients undergoing surgery and flurbiprofen axetil reduces postoperative pain scores but nausea, vomiting, and opioid consumption were similar in treated and untreated patients.[22] a randomized, controlled trial was conducted in patients with moderate-to-severe sore throat who received either flurbiprofen administered at the daily dose of 8.75 mg or lozenges administered at the daily dose of 9 mg. Reduction of pain, difficulty in swallowing, and throat swelling are lower (P-value < 0.05) in patients who received flurbiprofen.[23] and a prospective, randomized, placebo-controlled trial was conducted in patients undergoing post-endoscopic retrograde cholangiopancreatography pancreatitis who received either flurbiprofen axetil at the daily dose of 50 mg or placebo. Flurbiprofen axetil reduces pancreatitis more effectively (P-value < 0.05) than placebo.[24] The metabolism of flurbiprofen has been reviewed. Flurbiprofen is hydrolysed into 4'-hydroxy flurbiprofen by CYP2C9.[25] and is conjugated with glucuronic acid by UGT1A1, 1A3, 1A9. 2B4, and by UGT2B7 and UGT2B7 catalyses the glucuronidation of flurbiprofen at the highest activity.[26] Kai et al.[27] measured the concentration of flurbiprofen in human tissues. Flurbiprofen was administered orally at the daily dose of 40 mg twice-daily to 7 patients and topically at the dose of 20 mg twice-daily to 9 patients. The tissue concentration of flurbiprofen is higher following topical than oral administration and the concentration of flurbiprofen is higher in fat, tendon, and periosteum than in muscle.[27] Turner et al.[28] measured the concentration of flurbiprofen in the cadaveric human pharynx following the administration of 8.75 mg of flurbiprofen lozenge and spry formulations and the concentration of flurbiprofen is 3.8±0.9 µg and 41.5±19.1 µg following the administration of lozenge and spry formulations, respectively. The pharmacokinetics of flurbiprofen have been reviewed. Shin et al.[29]

Studied the pharmacokinetics of flurbiprofen in healthy volunteers according to the CYP2C9 genotype. The elimination half-life of flurbiprofen is 5.1±0.3 and 6.1±0.6 hours (P-value = 0.0004) in CYP2C9 extensive and poor, respectively. The total body clearance is higher in extensive metabolizers and the area under the concentration-time curve is lower in extensive metabolizers. The interaction of flurbiprofen with drugs has been reviewed. Omeprazole, an inhibitor of CYP2C9, reduces the elimination half-life of flurbiprofen.[30] brewed tea, grape juice, and cranberry juice are inhibitors of CYP2C9 and reduce the formation-rate of 4'-hydroxy flurbiprofen.[31] Maroof et al.[32] observed that flurbiprofen interacts with quinolone antacids, acetaminophen, fluconazole, dapsone and insulin and flurbiprofen increases the toxicity of warfarin, lithium, methotrexate, and cyclosporine. Lei et al.[33] observed that flurbiprofen axetil has a synergistic analgesic effect on sufentanyl thus flurbiprofen axetil reduces the amounts of sufentanyl required to achieve satisfactory analgesia. Flurbiprofen is a safe drug and only limited information is available about the toxicity induced by flurbiprofen. An old man undergoing cataract extraction received one drop of 0.03% flurbiprofen sodium in the left eye and flurbiprofen sodium caused intraoperative haemorrhage.[34] and a woman took 20 pieces of 100 mg of flurbiprofen to cause a suicide and flurbiprofen caused nausea and vomiting and after the gastric lavage and administration of carbon administered through a nasogastric probe and the patient was discharged from the hospital.[35] In conclusion, flurbiprofen is a propionic acid derivative and is a nonselective cyclooxygenase inhibitor. Flurbiprofen is approved for use in the symptomatic treatment of rheumatoid arthritis, juvenile arthritis, pain, ankylosing spondylitis, acute gout arthritis, tendinitis, bursitis, headache, postoperative dental pain, and primary dysmenorrhoea. In adults, the dose of flurbiprofen is 40 mg once-daily or twice-daily. The efficacy and safely of flurbiprofen, the prophylaxis with flurbiprofen, the treatment of patients with flurbiprofen, and the trials conducted with flurbiprofen have been reviewed. Flurbiprofen is hydroxylated into 4'-hydroxy flurbiprofen by CYP2C9 and is conjugated with glucuronic acid by different glucuronosyl transferases and UGT2B7 catalyses the glucuronidation of flurbiprofen at the highest activity. The concentration of flurbiprofen has been measured in human tissues following oral and topical administration and the concentration of flurbiprofen is higher following the topical than oral administration. The pharmacokinetics of flurbiprofen have been studied in extensive and poor CYP2C9 metabolizers and the elimination half-life is 5.1±0.3 and 6.1±0.6 hours (P-value = 0.0004) in extensive and poor metabolisers, respectively. The interaction of flurbiprofen with drugs and the toxicity induced by flurbiprofen have been reviewed. The aim of this study is to review the clinical pharmacology of flurbiprofen.

Conflict of interests

The authors declare no conflicts of financial interest in any product or service mentioned in the manuscript, including grants, equipment, medications, employments, gifts, and honoraria. This article is a review and drugs have not been administered to men or animals**.**

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