

## BIOWAIVER MONOGRAPHS OF DEXIBUPROFEN

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### ABSTRACT

Literature data are reviewed on the properties of dexibuprofen related to the biopharmaceutics classification system (BCS). Dexibuprofen was assessed to be a BCS class II drug. This article summarizes the main pharmacological effects, therapeutic applications, adverse drug reactions, drug-drug interactions, pharmacokinetic properties, physicochemical properties and BCS classification of dexibuprofen. Dexibuprofen is propionic acid derivatives. It is the active dextrorotatory enantiomer of ibuprofen.

**Keywords:** Dexibuprofen, Drug -drug interaction, Physicochemical properties.

### INTRODUCTION

A monograph based on literature data is presented on dexibuprofen concerning its properties related to the biopharmaceutics classification system (BCS). In brief, it is to Dexibuprofen data available from literature sources about dexibuprofen. Dexibuprofen is the most commonly used and most frequently prescribed NSAID. It is a non-selective inhibitor of cyclo-oxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2). It has a prominent analgesic and antipyretic role. Its effects are due to the inhibitory actions on cyclo-oxygenases, which are involved in the synthesis of prostaglandins. Prostaglandins have an important role in the production of pain, inflammation and fever.

### LITERATURE DATA

#### General Characteristics

Dexibuprofen chemical name is (2S)-2-[4-(2-methylpropyl)phenyl] propanoic acid (and its structure shown in Figure 1). S(+)-Ibuprofen can form salts with bases such as basic amino acids, examples are lysine and arginine. The lysine part enhances solubility of the ibuprofen in water and gastric solution (Dexibuprofen) obtained with half the dose racemic ibuprofen formulation<sup>1</sup>. It is the active dextrorotatory enantiomer of

ibuprofen. Most ibuprofen formulations contain a racemic mixture of dexibuprofen [(+)-ibuprofen] and (-)-ibuprofen. S(+)-Ibuprofen is over 100-fold more potent an inhibitor of cyclooxygenase-1 than R-Ibuprofen<sup>2</sup>. Dexibuprofen shows an equipotency with half of the racemic ibuprofen dose, and the introduction of dexibuprofen (Seractil) permits the prescription of lower doses<sup>3</sup>.

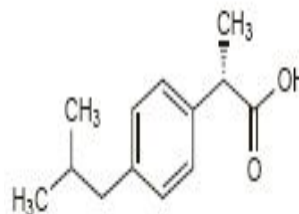


Fig. 1: Structure Of Dexibuprofen

#### Clinical Pharmacology of Dexibuprofen

Dexibuprofen is supplied as tablets with a potency of 200 to 400 mg<sup>4</sup>. The usual dose is 600 to 900 mg three times a day<sup>5</sup>. It is almost insoluble in water having pKa of 4.65<sup>6</sup>. It is well absorbed orally; peak serum concentrations are attained in 1 to 2 hours after oral administration. It is rapidly bio-transformed with a serum half life of 1.8 to

3.5 hours. The drug is completely eliminated in 24 hours after the last dose and eliminated through metabolism<sup>7,8</sup>. The drug is more than 99% protein bound, extensively metabolized in the liver and little is excreted unchanged<sup>9</sup>.

Although highly bound to plasma proteins (90-99%), displacement interactions are not clinically significant, hence the dose of oral anti-coagulants and oral hypoglycemic needs not be altered<sup>11</sup>. More than 90% of an ingested dose is excreted in the urine as metabolites or their conjugates, the major metabolites are hydroxylated and carboxylated compounds<sup>4,10</sup>.

Renal impairment also has no effect on the kinetics of the drugs, rapid elimination still occur as a consequence of metabolism<sup>12</sup>. The administration of ibuprofen tablets either under fasting conditions or immediately before meals yield quiet similar serum concentrations-time profile. When it is administered immediately after a meal, there is a reduction in the rate of absorption but no appreciable decrease in the extent of absorption.

### Therapeutic Applications

A low dose ibuprofen is as effective as aspirin and paracetamol for the indications normally treated with over the counter medications<sup>13</sup>. It is widely used as an analgesic, an anti inflammatory and an antipyretic agent<sup>14-15</sup>. Racemic ibuprofen and S(+) enantiomer are mainly used in the treatment of mild to moderate pain related to dysmenorrhea, headache, migraine, postoperative dental pain, management of spondylitis, osteoarthritis, rheumatoid arthritis and soft tissue disorder<sup>16</sup>. A number of other actions of NSAIDs can also be attributed to the inhibition of prostaglandins (PGs) or thromboxane synthesis, including alteration in platelet function (PGI<sub>2</sub> and Thromboxane), prolongation of gestation and labor (PGE<sub>2</sub>, PGF<sub>2A</sub>), gastrointestinal mucosal damage (PGI<sub>2</sub> and PGE<sub>2</sub>), fluid and electrolyte imbalance (renal PGs), premature closure of ductus arteriosus (PGE<sub>2</sub>) and bronchial asthma (PGs)<sup>17</sup>. The advantages of include greater dexibuprofen clinical efficacy, ease in dose optimization, less variability in therapeutic effects, all of these at half the

dose of ibuprofen. Greater peak analgesia was also seen with. It is indicated dexibuprofen for the relief of sign and symptoms of osteoarthritis, rheumatoid disorders such as osseous rheumatism, ankylosing spondylitis, juvenile arthritis, muscular rheumatism and degenerative joint disease. It is also used for the acute symptomatic treatment of painful menstruation, symptomatic treatment muscle pain, head ache and dental pain. Dexibuprofen has equal efficacy and comparable safety and tolerability<sup>19</sup> with celecoxib in the treatment of the osteoarthritis<sup>18</sup>. Dexibuprofen shows excellent tolerability, safety than other NSAID like diclofenac sodium, dexibuprofen has stronger pain reducing effect than racemic ibuprofen. Maximum Daily Dose of 3200mg<sup>18</sup>(adult) of Ibuprofen racemate is required, but dose required for dexibuprofen lysinate is 2692.5 mg of S+Ibuprofen lysinate equivalent to 1500mg of dexibuprofen 200-300mg every 4-6 hrs for the relief of pain. S(+) Ibuprofen is superior in anti-inflammatory action but equal to racemic ibuprofen in analgesic action.

Dexibuprofen is the single pharmacologically effective enantiomer of rac-ibuprofen. Racibuprofen and dexibuprofen differ in their physico-chemical properties, in terms of their pharmacological properties and their metabolic profiles. Several clinical trials and post-marketing surveillance studies were performed to broaden the findings on dexibuprofen. In the last 5 years 4836 patients have been exposed to dexibuprofen in clinical trials and PMS trials. Only in 3.7% of patients adverse drug reactions have been reported and 3 serious adverse drug reactions (0.06%) were observed. In the dose ratio of 1 : 0.5 (rac-ibuprofen vs. dexibuprofen) at least equivalent efficacy was proven in acute mild to severe somatic and visceral pain models. Dexibuprofen has proven at least comparable efficacy to diclofenac, naproxen and celecoxib and has shown a favourable tolerability. The results suggest that dexibuprofen processed in a special crystal form is a safe and effective treatment for different pain conditions.

### Indication

Dexibuprofen is indicated for the treatment of Pain and inflammation caused by osteoarthritis

Acute symptomatic treatment of pain during menstrual bleeding (Primary dysmenorrhoea) Mild to moderate pain, such as pain in the muscles and joints and toothaches. It may be used as an antipyretic to reduce fever.

### Contra-indications

Dexibuprofen should not be administered to Patients with hypersensitivity to Dexibuprofen or other non-steroidal anti-inflammatory drugs, Patients with active or suspected gastrointestinal ulcer or history of recurrent gastrointestinal ulcer, Patients who have gastrointestinal bleeding or other active bleedings or bleeding disorders, Patients with active Crohn's disease or active ulcerative colitis, Patients with severe renal dysfunction (GFR < 30ml/min), Patients with severely impaired hepatic function, Patients with hemorrhagic diathesis and other coagulation disorders, or patients receiving anticoagulant therapy, From the beginning of 6th month of pregnancy.

### Precautions

Symptoms or history of gastro-intestinal disease, asthma, impaired hepatic, cardiac or renal function. NSAID may mask infections or temporarily inhibit platelet aggregation. In late pregnancy, as with other NSAIDs, it should be avoided as it may cause premature closure of ductus arteriosus. Dexibuprofen should be used with caution in nursing mothers.

### Adverse Reactions

NSAIDs are widely used, frequently taken inappropriately and potentially dangerously<sup>20</sup>. Nevertheless, dexibuprofen exhibits few adverse effects<sup>21</sup>. The major adverse reactions include the effects on the gastrointestinal tract (GIT), the kidney and the coagulation system<sup>22</sup>. Based on clinical trial data, serious GIT reactions prompting withdrawal of treatment because of hematemesis, peptic ulcer,<sup>23</sup> and severe gastric pain or vomiting showed an incidence of 1.5% with ibuprofen compared

to 1% with placebo and 12.5% with aspirin<sup>24</sup>. Ibuprofen was a potential cause of GI bleeding<sup>25,26</sup>, increasing the risk of gastric ulcers and damage, renal failure, epistaxis<sup>27-30</sup>, apoptosis<sup>31</sup>, heart failure, hyperkalaemia<sup>32</sup>, confusion and bronchospasm<sup>33</sup>. It has been estimated that 1 in 5 chronic users (lasting over a long period of time) of NSAIDs will develop gastric damage which can be silent<sup>34</sup>. Other adverse effects of ibuprofen have been reported less frequently. They include thrombocytopenia, rashes, headache, dizziness, blurred vision and in few cases toxic amblyopia, fluid retention and edema. Patients who develop ocular disturbances should discontinue the use of dexibuprofen<sup>35</sup>. Effects on kidney (as with all NSAIDs) include acute renal failure, interstitial nephritis, and nephritic syndrome, but these very rarely occur<sup>36</sup>.

### Drug-Drug Interactions

Dexibuprofen has established drug interactions with NSAIDs which are both pharmacokinetic or pharmacodynamic in origin<sup>(37,38)</sup>. The most potentially serious interactions include the use of NSAIDs with lithium, warfarin, oral hypoglycemics, high dose methotrexate, antihypertensives, angiotensin converting enzyme inhibitors,  $\beta$ -blockers, and diuretics. Anticipation and care full monitoring can often prevent serious events when these drugs are used concomitantly<sup>39</sup>.

Observational studies and in-vivo experiments have raised concerns that the cardio protective effects of taking aspirin are blocked by ibuprofen which competitively inhibits aspirin's binding sites on platelets<sup>(41-43)</sup>. The pharmacodynamic interactions of aspirin and ibuprofen may not have a significant impact on patient outcomes<sup>45</sup>. Palmer et al. in 2003 suggested that NSAIDs interfere with certain antihypertensive therapies. Dexibuprofen caused a significant increase in systolic and diastolic blood pressure compared to placebo<sup>46</sup>. A case of life-threatening hypotension due to sinus arrest was described in a patient in whom exercise-induced hyperkalemia developed during a stable regimen that included verapamil, propranolol, and

ibuprofen<sup>47</sup>. Similar to other NSAIDs, ibuprofen is likely to decrease the diuretic and anti hypertensive actions of thiazides, furosemide and  $\beta$ -Blockers<sup>11</sup>.

Hence the administration of dexibuprofen caused a significant decrease in urinary output, inulin clearance, sodium excretion, osmolar clearance, free water clearance and urinary PGE<sub>2</sub> clearance<sup>89</sup>. Many overdose experiences have been reported in medical literature<sup>48</sup>. Ibuprofen may cause serious toxicity when overdosed, mainly in children on ingestion of 400 mg/kg or more. Maximum Daily Dose of 3200mg<sup>18</sup>(adult) of Ibuprofen racemate is required, but dose required for dexibuprofen lysinate is 2692.5 mg of S+Ibuprofen lysinate equivalent to 1500mg of dexibuprofen 200-300mg every 4-6 hrs for the relief of pain. S+ Ibuprofen is superior in anti-inflammatory action but equal to racemic ibuprofen in analgesic action. Dexibuprofen has a low acute toxicity and patients have survived after single doses as high as 54 g of racemic ibuprofen. Most overdoses have been asymptomatic. There is a risk of symptoms at doses >80 - 100 mg/kg racemic ibuprofen. The symptoms of high dose include seizures, apnea, and hypertension, as well as renal and hepatic dysfunction<sup>48-51</sup>. Ibuprofen has been implicated in elevating the risks of myocardial infarction, particularly among those chronically using high doses<sup>52-55</sup>.

Desmopressin and NSAIDs should not be used in combination in patients with bleeding disorders.<sup>56</sup> Coadministration of thiopurines and various NSAIDs (ketoprofen, dexibuprofen and ibuprofen) may lead to drug interactions.<sup>57</sup>

It has been observed that caffeine improves antinociceptive efficacy of some non-steroidal anti-inflammatory drugs (NSAIDs) in several experimental models, however, these effects have been questioned in humans. Caffeine is able to potentiate the antinociceptive effect of ibuprofen. This effect was greater than the maximum produced by morphine in the experimental conditions.<sup>58</sup> Caffeine also enhances the effectiveness of most analgesics, including ibuprofen. Comparison of the cumulative response scores revealed a trend toward a

greater response to ibuprofen-caffeine treatment of headaches.<sup>59</sup>

Gemfibrozil moderately increases the AUC of R-ibuprofen and prolongs its t (1/2), indicating that R-ibuprofen is partially metabolised by Cytochrome P2C8 (CYP2C8). The interconversion of R- to S-ibuprofen can explain the small effect of gemfibrozil on the t (1/2) of S-ibuprofen. However, the gemfibrozil-ibuprofen interaction is of limited clinical significance.<sup>60</sup>

*St. John's wort* is a popular herbal supplement that has been involved in various herb-drug interactions. *St. John's wort* treatment appears to significantly reduce the mean residence time of S-ibuprofen, no ibuprofen dose adjustments appear warranted when the drug is administered orally with *St. John's wort*, due to the lack of significant changes observed in ibuprofen area under the curve (AUC) and maximum concentration C (max) for either enantiomer.<sup>61</sup>

The effects of the antifungals voriconazole and fluconazole on the pharmacokinetics of S-(+) - and R-(-)-ibuprofen were studied by Hynninen et al. A reduction of ibuprofen dosage should be considered when ibuprofen is coadministered with voriconazole or fluconazole, especially when the initial ibuprofen dose is high due to the inhibition of the cytochrome P450 2C9-mediated metabolism of S-(+)-ibuprofen.<sup>62</sup>

The competitive binding characteristics of ibuprofen and *naproxen* with respect to the binding site on bovine serum albumin (BSA) were studied. Ibuprofen displaced *naproxen* and vice versa from its high affinity binding site (site II) and the displaced drug rebound to its low affinity binding site (site I) on BSA molecule.<sup>63</sup>

Anandamide, an endocannabinoid, is degraded by the enzyme fatty acid amide hydrolase which can be inhibited by nonsteroidal anti-inflammatory drugs (NSAIDs). The antinociceptive interaction between anandamide and ibuprofen was synergistic. The combination of anandamide with ibuprofen produced synergistic antinociceptive effects involving both cannabinoid CB<sub>1</sub> and CB<sub>2</sub> receptors.<sup>64</sup> A study by Kaminski et al. in 1998 showed

that all NSAIDs enhanced the protective activity of *valproate magnesium* against maximal electroshock-induced seizures. Only ibuprofen and piroxicam enhanced the anticonvulsive activity of diphenylhydantoin. Ibuprofen also decreased the effective dose 50 (ED<sub>50</sub> value) of valproate (for the induction of motor impairment). Thus, NSAIDs could enhance the protective activity of antiepileptics.<sup>65</sup>

#### **Posology and method of administration**

The dosage should be adjusted to the severity of the disorder and the complaints of the patient. During chronic administration, the dosage should be adjusted to the lowest maintenance dose that provides adequate control of symptoms.

#### **Adults**

The recommended dosage is 600 to 900 mg dexibuprofen daily, divided in up to three single doses. For the treatment of mild to moderate pain, initially single doses of 200 mg and daily Alpha 10 doses of 600 mg dexibuprofen are recommended. The maximum single dose is 400 mg dexibuprofen. The dose may be temporarily increased up to 1200 mg dexibuprofen per day in patients with acute conditions or exacerbations. The maximum daily dose is 1200 mg.

For dysmenorrhoea a daily dose of 600 to 900 mg Alpha 10, divided in up to three single doses, is recommended. The maximum single dose is 300 mg; the maximum daily dose is 900 mg.

#### **Children**

Dexibuprofen has not been studied in children and adolescents (< 18 years): Safety and efficacy have not been established and therefore it is not recommended in these age groups.

#### **100mg/5ml Solution**

Children and adolescents Dose: 10 to 15mg/kg daily in 2 to 4 divided doses

#### **Use in Elderly Patients**

It is recommended to start the therapy at the lower end of the dosage range. The dosage may be increased to that recommended for general population only after good general tolerance has been ascertained.

#### **Use in Patients with Hepatic dysfunction:**

Patients with mild to moderate hepatic dysfunction should start therapy at reduced doses and be closely monitored. Dexibuprofen should not be used in patients with severe hepatic dysfunction.

#### **Use in Patients with Renal dysfunction**

The initial dosage should be reduced in patients with mild to moderate impaired renal function. Dexibuprofen should not be used in patients with severe renal dysfunction.

#### **Over Dosage**

Dexibuprofen has a low acute toxicity and patients have survived after single doses as high as 54 g of racemic ibuprofen. Most overdoses have been asymptomatic. There is a risk of symptoms at doses > 80 - 100 mg/kg racemic ibuprofen.

#### **Storage**

Dexibuprofen should be kept in a tightly closed container, and out of reach of children. It should be stored in a cool, dry area and must be properly labeled.

#### **Physicochemical properties**

(S)-(+)-Ibuprofen (dexibuprofen) is one of the enantiomers of racemic ibuprofen which is a non-steroidal anti-inflammatory drug (NSAID), and it has a pharmaceutical activity in racemic compound. According to the literature, (S)-(+)-Ibuprofen has a solubility twice as high as that of the racemate, and its crystal structure, optical properties, thermodynamic properties are also different from the racemate.<sup>66</sup> Table 3.1 was the comparison between dexibuprofen and racemic ibuprofen. Its molecular weight 206.29, melting point is of 52 °C.

**Table: Physicochemical property of (S)-(+)-Ibuprofen.<sup>67</sup>**

Properties	Dexibuprofen	Racemic Ibuprofen
Space group	P21/C	P21
Density (g/cm <sup>3</sup> )	1.098	1.110
Melting point (°C)	52.1±0.3	75.3±0.3
Heat of fusion (J/g)	91±1	125±2
Solubility in water at 37 °C (mg/100ml)	11.8	4.8
Solubility in HCl at pH 1.5 and 37 °C (mg/100ml)	9.6	14.

### Solubility

Dexibuprofen is practically insoluble in water, but it is readily soluble in most organic solvents like methanol, methylene chloride, and acetone, and is soluble in aqueous solution of alkali hydroxides and carbonates. It is slightly soluble in a buffer medium of pH 6.8 and very slightly soluble in a buffer medium of pH 4.5.

Solubility values are shown in Table 1. In the literature only data at 20°C or room temperature were found<sup>10,11</sup>. BCS

classification requires data on the solubility at 37°C, these values were experimentally determined, for each media in triplicate. Dexibuprofen drug substance was suspended in medium and stirred for 24 h at 37°C and then stored for a further 24 h without agitation. In each case sediment on the bottom of the flask was observed. The dexibuprofen concentration in the clear supernatant was determined by UV-analysis.

These results are also shown in Table no:2.

Medium /pH	Solubility in mg/ml at 37°C±0.5°C	Solubility in 400mg/250ml at 37°C±0.5°C (as per BCS)
Purified water	0.06	7
1.2 buffer	0.03	4
4.5 acetate buffer	0.13	27
6.8 phosphate buffer	3.44	400
7.2 phosphate buffer	5.32	400

The equilibrium solubilities of dexibuprofen in pH 1.2 and pH 7.2 were reported to be 0.03 and 5.32 gm/ml respectively. Also it exhibits the pH dependent solubility.

### Partition coefficient

Calculation of the n-octanol-acid buffer distribution coefficient gave log P values at pH value 1.2.

### pKa

The pKa of dexibuprofen is in the range of 4.65.

## PHARMACOKINETICS PROPERTIES

### Absorption and Permeability

Absorbed primarily from the small intestine with maximum concentration ( $t_{max}$ ) of approximately 2 hours after oral administration. Food intake also affects the absorption rate of dexibuprofen, No Effect on AUC,  $t_{max}$  delayed by 0.7 hours,  $C_{max}$

decreased by 9.7%. which is likely due to food induced pH elevation in the stomach resulting in earlier in vivo dissolution of ibuprofen<sup>68</sup>. Rapid and complete absorption suggests a high permeability through the GI membrane.<sup>69,70</sup> Scintigraphic studies with sustained release products in humans indicate that ibuprofen absorption occurs throughout the GI tract following oral administration, which again supports a high permeability.<sup>70</sup> Rapid and complete absorption of ibuprofen was also reported from enteric coated microcapsules in humans administered as an oral suspension.<sup>71</sup> Similar to other NSAIDs, high permeability of ibuprofen and its enantiomers has been observed in rats, where increased GI permeability was observed because NSAIDs promote their own transport.<sup>72,73</sup> This observation may possibly explain the GI side effects and the damage of the GI membrane following oral

administration of high doses or upon long term oral usage of ibuprofen. High permeability of ibuprofen and its enantiomers has been also observed in Caco-2 cell cultures.

#### **Invitro dissolution studies**

The *invitro* dissolution studies of different formulations of Dexibuprofen-  $\beta$ -CD complexes were performed using USP XXII rotating basket method (USP,2005). The samples were placed in a hard gelatin capsules.900ml of 0.1N Hcl was used as dissolution media at  $37 \pm 0.5^\circ\text{C}$  and maintaining stirring speed at 50rpm. The samples were withdrawn and replaced with same volume of fresh dissolution media at different time intervals and estimated at 220nm by U.V. Spectrophotometer. The dissolution profile of Dexibuprofen in 0.1NHcl at 120min showed 43.09%. The inclusion complexes prepared by kneading method showed 78.15% and 88.01% for 1:1 and 1:2 molar ratios respectively whereas freeze dried showed 95.03% and 96.05% for 1:1 and 1:2 molar ratios respectively at 120 min. The freeze dried product of 1:2 showed marked increases in drug release compared with other methods.

#### **Polymorphism Study**

Polymorphism was a behavior that a solid had different molecular arrangements in a longrange order. Therefore, the interactions among molecules were different in a different polymorph. When Form transformation occurs, energy was needed for the re-arrangement of the molecules. So polymorphism could be identified by DSC. Besides, different polymorph gives different d-spacing in Bragg law, and PXRD could characterize it. According to the literature, S-Ibu had a melting point at about 49 to 53  $^\circ\text{C}$ , and the DSC analysis of solid re-crystallize by all good solvents showed that the peaks were in this arrange. This showed that S-Ibu re crystallized from good solvents by temperature cooling was isomorphism. Both S-Ibu and solid re crystallized had an endothermal peak in the range of 49 to 53  $^\circ\text{C}$ . Besides DSC data, PXRD was also an evidence of isomorphism to S-Ibu. The different solvents used only changed the aspect ratios and no new peaks appeared in

any of the DSC thermograms and XRD patterns.

#### **BCS Classification**

According to the present regulations, dexibuprofen is a BCS class II drug, showing high permeability and pH-dependent solubility, that is, a high solubility according to BCS requirements only above a certain pH value. The assignment of dexibuprofen to BCS Class II is supported by an observed in vitro in vivo correlation (IVIVC) where a rank order was found between dissolution characteristics and the rate of absorption, since IVIVC's are predicted for BCS Class II drugs.<sup>74</sup> Other worker classified dexibuprofen as BCS Class II also. One research group based its classification on solubility values, measured by the saturation-flask method, at different pH-values, and absorption permeability literature data; another research group based its classification on the solubility of ibuprofen in water, without taking into account the pH dependency, and calculated partition coefficients; the latter were shown to correlate with human intestinal permeability. Both of the current BCS Guidances allow the possibility for a biowaiver exclusively for BCS class I drugs. The limited solubility of dexibuprofen biowaiver criteria. However, at pH values near neutral, the solubility of dexibuprofen is sufficient to comply with criterion for high solubility: a dose solubility quotient of less than 250 mL. As these pH values are closer to those at the absorption sites in the small intestine they are therefore more relevant in terms of systemic absorption of dexibuprofen. Accordingly, ibuprofen may also fit in the newly proposed "intermediate solubility class" suggested for acids and bases that are highly soluble at either physiologically relevant pH 1.2 or 6.8. Current publications also suggest pH-dependent soluble, highly permeable, weak acidic ionizable drug compounds should be handled like BCS class I drugs. This evaluation is supported by Rinaki et al.<sup>75</sup> who emphasized the dynamic character of the absorption process, as drug dissolution is promoted by high permeability for highly permeable acidic NSAIDs like ibuprofen.

**CONCLUSION**

Dexibuprofen is suitable for self medication with regards to its relatively wide spectrum of indication, good tolerance and safety. The Dexibuprofen is more potent than racemic formulation of ibuprofen with respect to its analgesic and anti inflammatory properties, and it produced less acute gastric damage. Therefore, administration of the racemic formulation should be avoided if it is not essential for the therapeutic activity expected.

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