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Galaxy Publication

Pharmacokinetics and Safety of Imrecoxib, a Novel Selective Cyclooxygenase-2 Inhibitor, in Elderly Healthy Subjects: A Comparative Study

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ABSTRACT

Imrecoxib is a novel, moderately selective cyclooxygenase-2 (COX-2) inhibitor with anti-inflammatory and analgesic properties, commonly used in patients with osteoarthritis. However, pharmacokinetic data to guide its use in the elderly are currently lacking.This study aimed to evaluate the pharmacokinetics of imrecoxib and its primary metabolites and to assess its safety in healthy elderly subjects.Nineteen healthy participants, including 10 non-elderly and 9 elderly individuals, received a single 100 mg oral dose of imrecoxib under fasting conditions. Pharmacokinetic parameters, safety, and tolerability were analyzed.Following a single 100 mg oral dose, imrecoxib was absorbed with a median time to peak plasma concentration (Tmax) of approximately 2 hours. Plasma concentration–time profiles of imrecoxib (M0) showed greater interindividual variability among elderly participants compared to non-elderly ones. In elderly subjects, peak plasma concentrations (Cmax) of M0, its hydroxyl metabolite M1, and carboxyl metabolite M2 increased by 39%, 21%, and 17%, respectively, while the area under the concentration–time curve from 0 to t (AUC0–t) rose by 34%, 13%, and 27%, respectively, compared with non-elderly subjects. The 90% confidence intervals for the geometric mean ratios of Cmax, AUC0–t, and AUC0–∞ of M0, M1, and M2 between the groups fell outside the 80–125% range, suggesting these pharmacokinetic parameters were not fully equivalent. Nevertheless, statistical comparison of M0, M1, and M2 pharmacokinetics revealed no significant differences ($P > 0.05$). Imrecoxib was well tolerated in both age groups, with particularly favorable gastrointestinal and cardiovascular safety profiles.The pharmacokinetic and safety data indicate that elderly healthy subjects do not require dose adjustments when using imrecoxib.

Keywords: Elderly, Cyclooxygenase-2 inhibitor, Imrecoxib, Safety, Pharmacokinetics

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Introduction

Osteoarthritis (OA) is a chronic degenerative disorder of the musculoskeletal system and a leading cause of pain and disability, particularly among the elderly [1–4]. Aging is recognized as the primary risk factor for OA development [2–4], and its global prevalence has risen markedly over recent decades [5]. Evidence suggests that oral non-steroidal anti-inflammatory drugs (NSAIDs) are commonly recommended pharmacological treatments for OA [1, 4], as they mainly act by inhibiting cyclooxygenase (COX) enzymes to reduce inflammation and alleviate pain [6, 7].

COX exists in two isoforms, COX-1 and COX-2. Based on their COX selectivity, oral NSAIDs can be categorized as non-selective inhibitors, which target both COX-1 and COX-2, and selective COX-2 inhibitors [6, 8, 9]. Non-selective COX inhibitors provide anti-inflammatory and analgesic effects primarily through COX-2 inhibition but can also increase gastrointestinal adverse events due to COX-1 inhibition [6, 8, 10]. In contrast, selective COX-2 inhibitors preserve the protective gastrointestinal functions mediated by COX-1, thereby lowering the risk of gastrointestinal complications [6, 8, 10]. Accordingly, non-selective COX inhibitors are generally recommended for patients without contraindications such as gastrointestinal disorders or hepatic and renal insufficiency, whereas

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selective COX-2 inhibitors, such as celecoxib, may be preferred for individuals at higher risk of gastrointestinal comorbidities, as suggested by multiple clinical guidelines [1, 4, 6].

However, excessive COX-2 inhibition can disrupt the balance between prostacyclin (PGI2) and thromboxane A2 (TXA2), and prolonged use of COX-2 inhibitors may increase the risk of cardiovascular events, a factor that led to the global withdrawal of rofecoxib in 2004 [11, 12]. Therefore, an ideal selective COX-2 inhibitor should not exhibit extreme selectivity but should instead maintain a balanced inhibition of COX-2 and COX-1, preserving the functional equilibrium between PGI2 and TXA2 [13].

Imrecoxib is a novel, moderately selective COX-2 inhibitor with pharmacological effects comparable to celecoxib [14–16]. It exerts anti-inflammatory activity through moderate suppression of COX-2 mRNA expression [17] and is widely used in orthopedic practice, particularly for knee OA [16]. Phase II and III clinical trials have demonstrated that imrecoxib significantly improves clinical symptoms in knee OA patients, with efficacy similar to that of celecoxib [14, 15]. In humans, imrecoxib is metabolized first to the hydroxylated metabolite M1 and then oxidized to the carboxylated metabolite M2 [18–20], with the major metabolic pathway illustrated in **Figure 1** [18, 21].

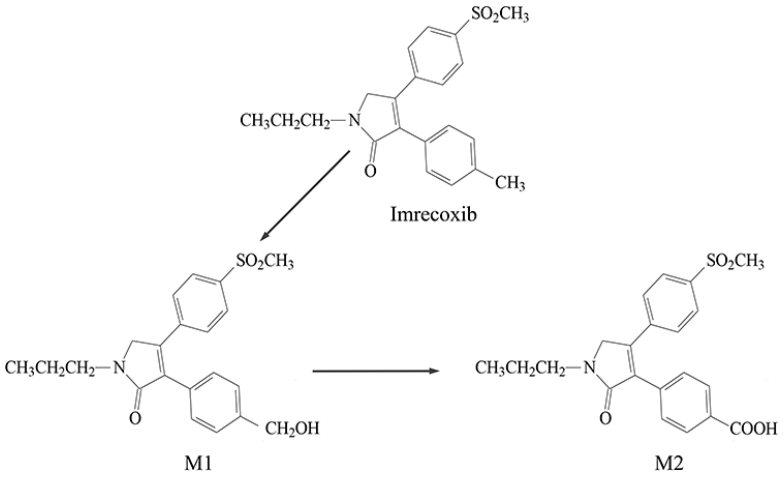

Figure 1. The major metabolic process of imrecoxib

The proportion of elderly individuals is rising significantly worldwide [22]. As aging leads to the gradual decline of various tissues and organ functions, it is crucial to consider age-related changes in drug pharmacokinetics and pharmacodynamics to prevent inappropriate medication use [23–27]. Previous studies have examined the pharmacokinetics of imrecoxib in healthy subjects, as well as in patients with renal or hepatic impairment [21, 28]; however, there is no research evaluating the pharmacokinetics, safety, or tolerability of imrecoxib specifically in the elderly, limiting evidence-based guidance for its use in this population. Therefore, the present study aimed to provide the first evidence supporting the rational use of imrecoxib in elderly individuals by comparing the pharmacokinetic profiles of imrecoxib and its primary metabolites (M1 and M2), along with its safety and tolerability, between elderly and non-elderly healthy subjects.

Materials and Methods

Study design

This single-center, single-dose, open-label, parallel-controlled Phase I clinical trial was designed to include 20 healthy Chinese participants, with 10 subjects in both the non-elderly and elderly groups. The complete study flowchart is presented in **Figure 2**.

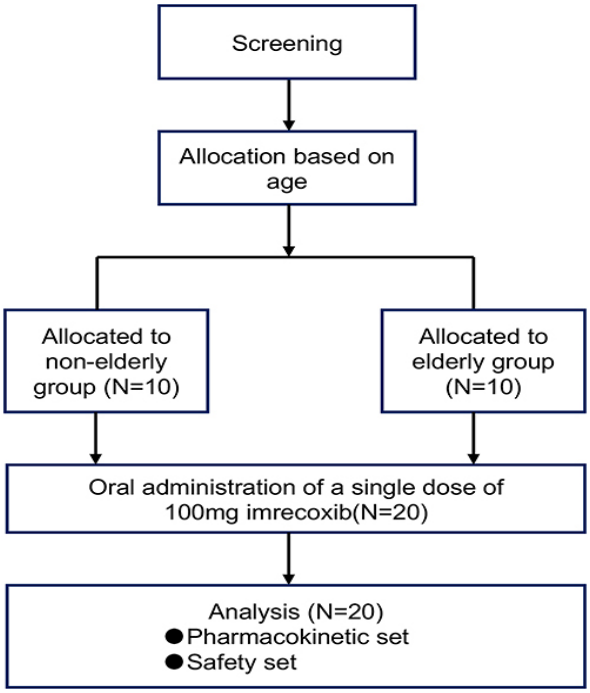

Figure 2. The flowchart of the study.

The study was carried out in accordance with the ICH-GCP guidelines and the Declaration of Helsinki. The protocol and informed consent forms (ICFs) were approved by the Independent Ethics Committee of West China Hospital, Sichuan University (No. 2015–79). All participants provided written informed consent prior to any study-related procedures. The trial was also registered with the World Health Organization International Clinical Trials Registry Platform (ChiCTR2100051644).

Study population

Eligible participants were healthy Chinese adults (male:female ratio 1:1) aged 18–85 years, with a body mass index (BMI) between 19 and 28 kg/m². Subjects aged 18–64 years were assigned to the non-elderly group (Group A), while those aged 65–85 years were assigned to the elderly group (Group B). Non-elderly participants with clinically significant abnormalities in medical history, physical examination, laboratory tests (including hematology, blood biochemistry, urinalysis, hepatitis B and C serology, HIV and syphilis screening, alcohol, smoking, or drug abuse testing), 12-lead ECG, chest X-ray, or abdominal ultrasound were excluded. Elderly participants with well-controlled chronic conditions that did not interfere with study endpoints were eligible. Additional exclusion criteria included known allergies to imrecoxib or its components, and history of cardiovascular, hepatic, renal, gastrointestinal, immune, hematologic, endocrine, metabolic, oncologic, neuropsychiatric, or other disorders potentially affecting drug absorption, distribution, metabolism, or excretion, as well as use of investigational drugs, including placebo, within 30 days.

Drug administration and pharmacokinetic sampling

Eligible participants were admitted to the Phase I clinical trial ward at West China Hospital on Day −1 and fasted overnight for 10 hours. On Day 1, each subject received a single oral dose of 100 mg imrecoxib with 240 mL of water under fasting conditions; water was withheld for 1 hour prior to dosing.

Blood samples (~3 mL) were collected for pharmacokinetic analysis at the following timepoints: pre-dose (within 60 minutes) and 0.5, 1.0, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48, and 72 hours post-dose. Samples were collected into EDTA tubes, centrifuged at 3000 rpm for 10 minutes at 4°C within 30 minutes of collection, and plasma was divided into three tubes (350 µL each) for storage at −70°C until analysis. Imrecoxib tablets (100 mg) were manufactured by Jiangsu Hengrui Pharmaceuticals Co., Ltd. (Jiangsu, China).

Safety and tolerability assessment

Participants were monitored in the clinical trial ward for 72 hours post-dose. Tolerability was assessed through monitoring adverse events (AEs), physical examinations, laboratory tests (hematology, blood biochemistry, urinalysis), and 12-lead ECGs. All laboratory analyses were performed at the CAP-accredited clinical laboratory of West China Hospital.

Assay of imrecoxib and metabolites

Plasma concentrations of imrecoxib (M0) and its metabolites M1 and M2 were quantified using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Chromatography was performed on an ACQUITY I Class UPLC system (Waters, Milford, MA, USA) with an Eclipse Plus C18 column (100×4.6 mm, 3.5 μm, Agilent, Palo Alto, CA, USA). Mass spectrometry was conducted using a Triple Quad 5500 system (Applied Biosystems, Foster City, CA, USA). Standards and internal standard (IS) BAP385 were provided by Jiangsu Hengrui Pharmaceuticals. Sample preparation for M1 and IS involved spiking 100 μL plasma with methanol-water, IS, and acetonitrile, followed by vortexing, centrifugation, and addition of ammonium acetate with formic acid prior to LC-MS/MS injection. Similar preparation was applied for M0 and M2 with adjusted mobile phase ratios. The multiple reaction monitoring (MRM) transitions were 370.2→278.2 for M0, 386.2→278.2 for M1/IS, and 400.2→236.2 for M2. Optimized MS parameters included ion source gas 50 psi, curtain gas 30 psi, collision gas 8 psi, declustering potential 80 V, corona discharge current 3 μA, source temperature 500°C, spray voltage 5000 V, and collision energies 32, 29, and 40 V for M0, M1/IS, and M2, respectively. Data were processed with Analyst 1.6.2 software.

Pharmacokinetic and statistical analysis

Pharmacokinetic parameters were calculated using non-compartmental analysis in Phoenix WinNonlin Version 6.4 (Pharsight, Mountain View, CA, USA). Parameters included Cmax, Tmax, AUC0–t, AUC0–∞, elimination half-life (t1/2), volume of distribution/bioavailability (Vz/F), and clearance/bioavailability (CL/F). Statistical analyses were performed using SPSS Version 11.5 (IBM, Chicago, IL, USA) and SAS Version 9.4 (SAS Institute, Cary, NC, USA). Independent-samples t-tests (for normally distributed data) or nonparametric tests (for non-normal data) were used to compare groups. Two-tailed P-values <0.05 were considered statistically significant. Geometric means of Cmax and AUC were calculated, with equivalence defined as 90% confidence intervals of the geometric mean ratios falling within 80–125%.

Results and Discussion

Study population

The research aimed to enroll 20 participants and screened a total of 28 individuals. Nineteen subjects met the eligibility criteria and were enrolled, including 10 non-elderly participants (5 males and 5 females) and 9 elderly participants (4 males and 5 females). All enrolled subjects completed the study according to the protocol and were included in both the pharmacokinetic and safety analyses. Within the elderly group, two participants had a history of hypertension and were receiving antihypertensive therapy with amlodipine besylate and nifedipine sustained-release tablets, respectively. Detailed demographic characteristics of the study population are presented in **Table 1.**

Table 1. Demographics of enrolled subjects

Characteristic	Non-Elderly Group (N=10)	Elderly Group (N=9)	Total (N=19)
Age (years)	33.0±8.5	67.4±1.9	49.3±18.7
Gender (male/female)	5/5	4/5	9/10
Weight (kg)	59.25±6.61	61.67±4.24	60.39±5.60
Height (m)	1.618±0.083	1.586±0.074	1.603±0.078
BMI (kg/m^2)	22.679±2.293	24.614±2.371	23.596±2.472
Medical history (yes/no)	0/10	2/7	2/17
Concomitant treatment (yes/no)	0/10	2/7	2/17

Note: Data are presented as mean ± standard deviation (Mean ± SD), except for variables such as gender, medical history, and concomitant treatments, which are expressed as percentages.

Abbreviation: BMI, body mass index.

Assay validation

Representative chromatograms for imrecoxib (M0), M1, M2, and the internal standard (IS) are presented in **Figure 3**. Calibration curves were linear across the following ranges: 0.100–40.0 ng/mL for M0, 0.200–80.0 ng/mL for M1, and 2.00–800 ng/mL for M2. Intra-day relative standard deviation (RSD) values for quality control (QC) samples at low, medium, and high concentrations were below 6.2% for M0, 4.3% for M1, and 5.0% for M2. The relative error (RE) for QC samples at these concentrations ranged from −7.1% to 3.9% for M0, −9.4% to −8.1% for M1, and −5.4% to 0.0% for M2.

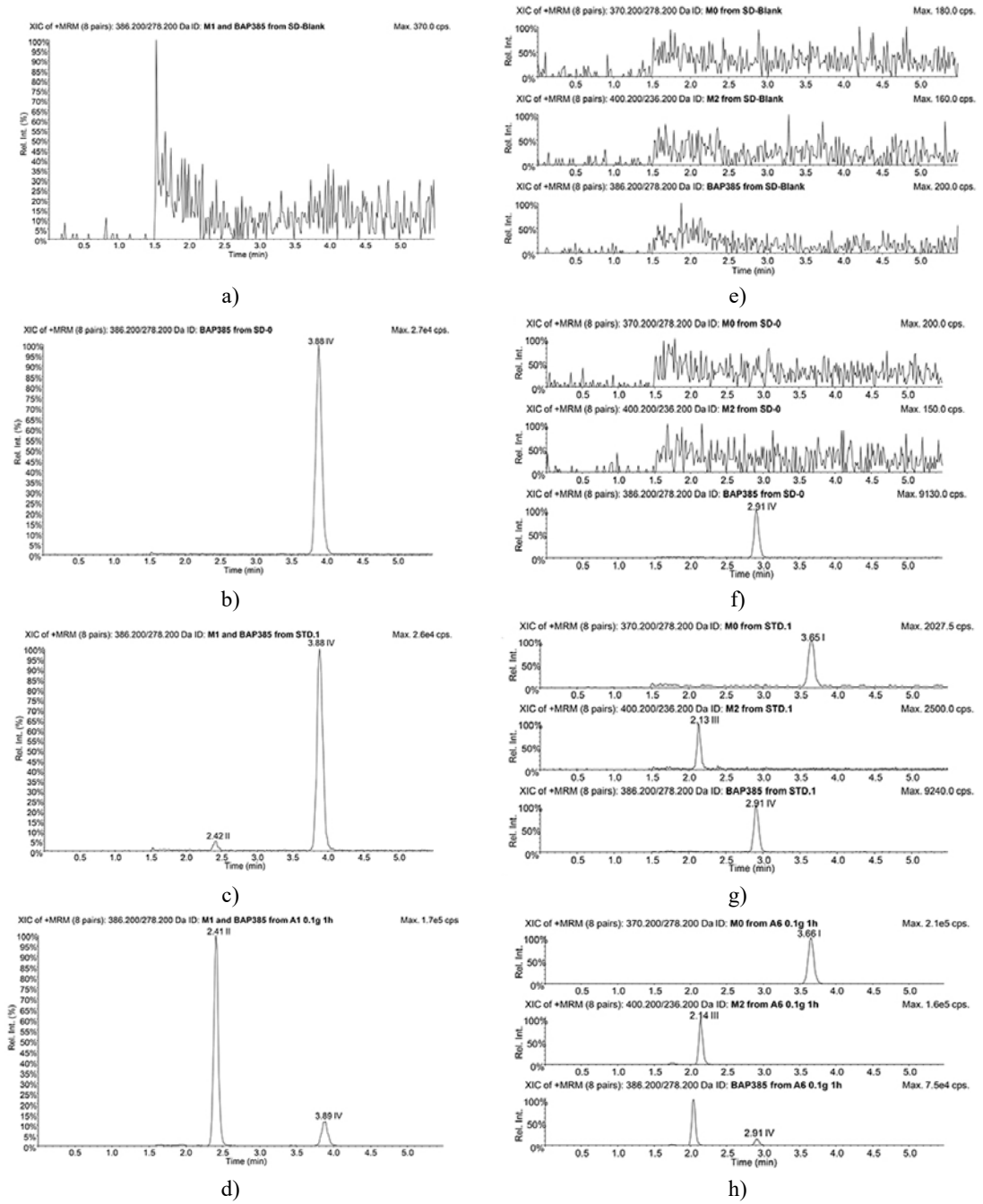

Figure 3. Typical chromatograms for imrecoxib (M0), its metabolites M1 and M2, and the internal standard (IS) are illustrated. Panels (a–d) correspond to M1 and IS: (a) blank plasma; (b) blank plasma spiked with IS; (c) blank plasma containing M1 and IS at the lower limit of quantitation (LLOQ); and (d) plasma collected 1 hour after a 100 mg oral dose of imrecoxib. Panels (e–h) depict M0, M2, and IS: (e) blank plasma; (f) blank

plasma with IS; (g) blank plasma spiked with M0, M2, and IS at their LLOQ; and (h) plasma collected 1 hour post-dose. Peaks I–IV represent M0, M1, M2, and IS (BAP385), respectively.

Abbreviations: IS, internal standard; LLOQ, lower limit of quantitation.

Pharmacokinetic characteristics

Plasma concentration–time profiles for individual subjects and group means of imrecoxib (M0) and its metabolites M1 and M2 are shown for both non-elderly and elderly participants after a single 100 mg oral dose **(Figure 4).** Imrecoxib was rapidly absorbed, reaching a median Tmax of 2 hours. Compared with non-elderly participants, elderly subjects displayed greater variability in M0 plasma levels **(Figures 4a and 4b)**, and their mean concentration–time curves indicated higher overall exposure to M0 **(Figure 4c)**. The complete pharmacokinetic parameters and intergroup comparisons are provided in **Table 2**.

Table 2. Results of plasma pharmacokinetics of imrecoxib (M0), M1 and M2

Analyze	Pharmacokinetic	Non-Elderly Group	Elderly Group	*P* value
		Mean ± SD (CV%)	Mean ± SD (CV%)	
M0	C_{max} (ng/mL)	13.9±10.8(77.2)	30.7±37.5(122.2)	0.226
	*T_{max} (h)	2.00(0.500–6.00)	2.00 (4.32–28.9)	0.427
	AUC_{0-t} (h*ng/mL)	163±110(67.5)	309±370(119.7)	0.283
	$AUC_{0-\infty}$ (h*ng/mL)	173±107(61.9)	315±368(116.9)	0.293
	$t_{1/2}$ (h)	10.9±6.07(55.7)	13.0±7.31(56.3)	0.508
	V_z/F (L)	12,300±8780(71.4)	17,400±20,000(114.5)	0.495
	CL/F (L/h)	765±366(47.9)	789±784(99.4)	0.935
M1	C_{max} (ng/mL)	36.6±14.0(38.1)	44.2±16.6(37.5)	0.294
	*T_{max} (h)	2.00(1.00–6.00)	2.00 (1.50–6.00)	0.643
	AUC_{0-t} (h*ng/mL)	370±97.1(26.2)	427±123(28.9)	0.275
	$AUC_{0-\infty}$ (h*ng/mL)	393±103(26.1)	443±126(28.4)	0.355
	$t_{1/2}$ (h)	9.25±4.38(47.3)	11.5±5.77(50.4)	0.349
	V_z/F (L)	3482±1445(41.5)	4064±2205(54.3)	0.501
	CL/F (L/h)	273±83(30.4)	255±121(47.5)	0.696
M2	C_{max} (ng/mL)	130±47.5(36.6)	148±37.5(25.4)	0.376
	*T_{max} (h)	1.50(1.00–3.00)	2.00 (1.50–6.00)	0.042#
	AUC_{0-t} (h*ng/mL)	1180±340(28.9)	1580±662(41.8)	0.130
	$AUC_{0-\infty}$ (h*ng/mL)	1300±449(34.5)	1740±734(42.2)	0.129
	$t_{1/2}$ (h)	9.65±4.02(41.7)	12.3±8.15(66.2)	0.395
	V_z/F (L)	1094±281(25.7)	1029±496(48.2)	0.724
	CL/F (L/h)	85±29(34.1)	71±40(56.3)	0.399

Notes: Data are expressed as Mean ± SD (with coefficient of variation, CV%), except for *Tmax, which is reported as median (range). #A difference between groups was considered statistically significant at $P < 0.05$.

Abbreviations: Cmax, peak plasma concentration; Tmax, time to reach Cmax; AUC0–t, area under the plasma concentration–time curve from 0 to the last measurable point; AUC0–∞, area under the plasma concentration–time curve from 0 to infinity; t1/2, elimination half-life; Vz/F, apparent volume of distribution; CL/F, apparent clearance; SD, standard deviation.

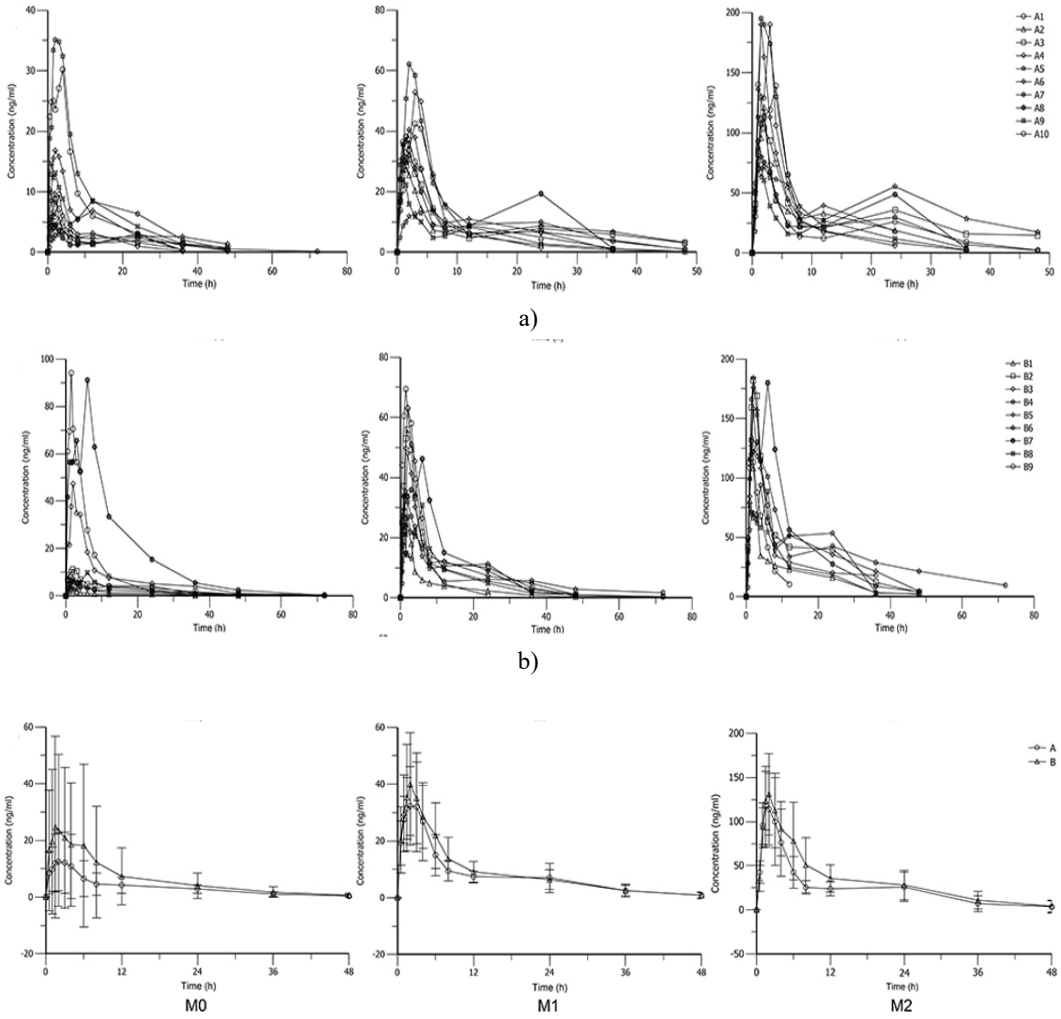

Figure 4. Plasma concentration–time profiles for imrecoxib (M0) and its metabolites M1 and M2 are displayed for both individual subjects and group means. Panels (a) and (b) show individual curves for the non-elderly (a1–a10) and elderly (b1–b9) participants, respectively, while panel (c) presents the average concentration–time profiles for the two groups.

Pharmacokinetic comparisons between groups were performed using independent-samples t-tests, except for Tmax, which was evaluated with the nonparametric Mann–Whitney U-test. The time to reach maximum plasma concentration (Tmax) for M2 was significantly longer in the elderly group ($P < 0.05$), whereas no significant differences were observed for other pharmacokinetic parameters of M0, M1, or M2 ($P > 0.05$).

Additionally, the ratios of geometric means and corresponding 90% confidence intervals (CIs) for Cmax, AUC0–t, and AUC0–∞ were determined. As summarized in **Table 3**, elderly subjects exhibited 39%, 21%, and 17% higher Cmax values for M0, M1, and M2, respectively, and AUC0–t values increased by 34%, 13%, and 27% for the same compounds. Since the 90% CIs of the geometric mean ratios for these parameters fell outside the 80–125% equivalence range, the exposures of imrecoxib and its metabolites cannot be considered fully equivalent between elderly and non-elderly participants.

Table 3. Geometric mean ratio and its 90% CI of main pharmacokinetic parameters of imrecoxib (M0), M1 and M2

Analyze	Pharmacokinetic	Geometric Mean		Geometric Mean Ratio (%)	
		Group A (N=10)	Group B (N=9)	B/A	90% CI

M0	C_{max} (ng/mL)	10.8	15.0	139	(60.9, 317)
	AUC_{0-t} (h*ng/mL)	137	183	134	(67.4, 265)
	$AUC_{0-\infty}$ (h*ng/m)	148	193	130	(67.5, 250)
M1	C_{max} (ng/mL)	34.0	41.3	121	(87.5, 169)
	AUC_{0-t} (h*ng/mL)	358	406	113	(87.9, 146)
	$AUC_{0-\infty}$ (h*ng/m)	380	421	111	(85.8, 144)
M2	C_{max} (ng/mL)	122	143	117	(89.6, 153)
	AUC_{0-t} (h*ng/mL)	1130	1440	127	(93.2, 174)
	$AUC_{0-\infty}$ (h*ng/m)	1230	1580	128	(91.3, 179)

Notes: Group A refers to the non-elderly cohort, and Group B refers to the elderly cohort. Cmax and AUC values between the two groups were considered equivalent if the 90% confidence intervals (CIs) of their geometric mean ratios fell within 80–125%.
Abbreviations: Cmax, peak plasma concentration; AUC0–t, area under the plasma concentration–time curve from 0 to the last measurable point; AUC0–∞, area under the plasma concentration–time curve from 0 to infinity; CIs, confidence intervals.

Safety and tolerability

Adverse events (AEs) observed in the study are summarized in **Table 4**. In the non-elderly group, 2 participants (20.0%) experienced a total of 4 AEs, while in the elderly group, 2 participants (22.2%) experienced a total of 2 AEs. Among these, one AE in the non-elderly group—elevated blood glucose—was classified as an adverse drug reaction (ADR). In the elderly group, increased levels of aspartate transaminase and blood bilirubin were both considered ADRs.

Table 4. Summarization of all the adverse events

	Non-Elderly Group (N=10)				**Elderly Group (N=9)**			
	Incidence (%)	**Severity Grade**			**Incidence (%)**	**Severity Grade**		
		I	**II**	**III**		**I**	**II**	**III**
All adverse events	2(20.0%)	2	0	0	2(22.2%)	2	0	0
Acute upper respiratory infection	1(10.0%)	1	0	0	0(0.0%)	0	0	0
White blood cell increased	1(10.0%)	1	0	0	0(0.0%)	0	0	0
Aspartate transaminase increased	0(0.0%)	0	0	0	1(11.1%)	1	0	0
Blood bilirubin increased	0(0.0%)	0	0	0	1(11.1%)	1	0	0
Blood glucose increased	1(10.0%)	1	0	0	0(0.0%)	0	0	0
Fibrinogen decreased	1(10.0%)	1	0	0	0(0.0%)	0	0	0

All reported adverse events (AEs) were mild and resolved spontaneously without medical intervention. No gastrointestinal, cardiovascular, or renal side effects related to cyclooxygenase inhibition were observed. In the non-elderly group, an increase in blood glucose was classified as an adverse drug reaction (ADR), while in the elderly group, elevated aspartate transaminase and blood bilirubin were considered ADRs. Overall, imrecoxib was well tolerated in both age groups, demonstrating a favorable safety profile.

Imrecoxib was developed under the principle of "moderate COX-2 inhibition" to maintain a balance between prostacyclin (PGI2) and thromboxane A2 (TXA2) activity [14–16, 29]. This study represents the first investigation into the influence of age on the pharmacokinetics of imrecoxib (M0) and its primary metabolites (M1 and M2), as well as the safety and tolerability of imrecoxib in healthy elderly individuals, providing guidance for its clinical use in this population.

Following oral administration, imrecoxib undergoes extensive first-pass metabolism, with M0 converted predominantly into M1 and then M2 via liver enzymes including CYP2C9, CYP2D6, and CYP3A4 [18, 29]. The drug is primarily excreted in urine as M2 and its glucuronide conjugates [29–31]. Both M1 and M2 exhibit moderate COX-1/COX-2 selectivity [19]. Previous studies have demonstrated linear pharmacokinetics of imrecoxib over a wide dose range (30–200 mg), with M0 and M1 showing similar pharmacokinetic profiles, while

plasma concentrations of M2 were approximately eightfold higher [29]. Interindividual variability was moderate, and Tmax for all three compounds was around 2 hours [29].

Consistent with these findings, in our study, a single 100 mg dose under fasting conditions resulted in M0 absorption with a median Tmax of 2 hours. Elderly subjects exhibited greater variability in individual concentration–time curves compared with non-elderly participants. Plasma Cmax of M0, M1, and M2 increased by 39%, 21%, and 17%, respectively, and AUC0–t increased by 34%, 13%, and 27% in elderly participants. Although geometric mean ratios for Cmax, AUC0–t, and AUC0–∞ fell outside the 80–125% equivalence range, the differences in key pharmacokinetic parameters, including Cmax, AUC0–t, AUC0–∞, Vz/F, and CL/F, were not statistically significant except for the prolonged Tmax of M2 in the elderly.

Age-related physiological changes may explain these observations. Reduced gastrointestinal motility, mucosal integrity, blood flow, and gastric acid secretion can slow drug absorption, while decreased renal perfusion may prolong drug half-life and delay elimination [23, 26, 32]. Furthermore, the activities of cytochrome enzymes such as CYP2C9 and CYP3A4 decrease with age, which could increase plasma concentrations of imrecoxib and its metabolites [20, 23, 27]. Interindividual variability in liver enzyme activity, particularly in older adults, may also contribute to the observed variability in pharmacokinetics.

Despite these age-related increases in exposure, statistical analysis showed no significant impact of age on the pharmacokinetics of imrecoxib, indicating that dose adjustments are not necessary for otherwise healthy elderly individuals. However, patients with renal impairment have been shown to exhibit markedly higher M2 exposure and reduced clearance, highlighting the need for dose modification in such populations [28, 33]. Clinicians should therefore consider comorbid conditions that substantially affect drug absorption, distribution, metabolism, or excretion when prescribing imrecoxib to elderly patients.

Imrecoxib's IC50COX-1/IC50COX-2 ratio of 6.39 (77% of celecoxib) suggests a lower incidence of adverse events compared with rofecoxib, whose ratio exceeds 213 [17, 29, 34]. Clinical studies and Phase IV trials have confirmed the efficacy of imrecoxib in managing inflammation and pain in osteoarthritis, with a favorable gastrointestinal and cardiovascular safety profile [16, 35, 36].

In our study, reported ADRs were mild and resolved without intervention, further supporting the tolerability of imrecoxib in both non-elderly and elderly healthy subjects. Limitations include the inclusion of two elderly participants with well-controlled hypertension on amlodipine or nifedipine, whose potential influence on pharmacokinetics is unknown. Additionally, the relatively small sample size may limit statistical power. Future studies with larger populations are needed to evaluate the effects of common geriatric conditions and concomitant medications on imrecoxib pharmacokinetics and pharmacodynamics.

Conclusion

While elderly subjects showed modestly higher plasma exposures of imrecoxib and its main metabolites compared with non-elderly subjects, these differences were not statistically significant. Imrecoxib was well tolerated in elderly healthy individuals, suggesting that no routine dose adjustment is required. Nevertheless, dose optimization may be warranted in elderly patients with chronic conditions that substantially alter drug absorption, distribution, metabolism, or excretion.

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Conflict of Interest: None

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Ethics Statement: None

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