Journal of Biosciences and Medicines, 2026, 14(2), 22-32
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

The Anticoagulant Effect of Ibuprofen and Interactions Including Anticoagulants

Dennis Flanagan[1,2]

[1]Jacksonville University, Jacksonville, FL, USA
[2]Department of Dental Medicine, Lugano University of Switzerland, Lugano, Switzerland
Email: dffdds@comcast.net, dflanag1@ju.edu

How to cite this paper: Flanagan, D. (2026) The Anticoagulant Effect of Ibuprofen and Interactions Including Anticoagulants. *Journal of Biosciences and Medicines*, **14**, 22-32.
https://doi.org/10.4236/jbm.2026.142003

Received: December 8, 2025
Accepted: January 26, 2026
Published: January 29, 2026

Abstract

Ibuprofen (IBU) is a non-steroidal anti-inflammatory drug (NSAID). A clinician wishing to appropriately control more moderate to severe pain may consider a combination of orally administered ibuprofen (IBU) and acetaminophen for pain control. In dentistry, it is commonly recommended to take oral IBU 400 - 800 mg and acetaminophen 325 - 1000 mg to control postoperative pain following third molar extraction(s). This combination can avoid the use of a narcotic prescription for pain control. However, many patients are taking anticoagulants for a variety of medical conditions and are told not to take IBU, fearing an additive effect of IBU with the anticoagulant. This paper addresses the anticoagulant effects of IBU when administered as a single agent and the interactions with orally administered anticoagulant, antiplatelet, or antithrombotic agents. Ibuprofen may be taken by patients taking anticoagulants for 2 - 5 days without significant interaction. Nonetheless, the prudent clinician should ensure the patient is compliant and that alternative pain medications have been considered.

Keywords

NSAID, Hemorrhage, Pain, Dental, Coagulation, Anticoagulant

1. Introduction

Ibuprofen (IBU) is an over-the-counter (OTC) non-steroidal anti-inflammatory drug (NSAID) (**Figure 1**). It is sold as the racemic S enantiomer to produce the desired pharmacologic action. IBU has an elimination half-life of 2 hours [1] [2]. IBU is used to treat fever, pain, and inflammation [3]-[5]. IBU may not be as effective an anti-inflammatory agent when compared to other NSAIDs [6]. Literature on the safety of IBU is plentiful [1]. NSAIDs, when combined with

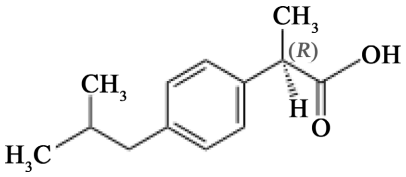

Figure 1. Schematic of the chemical structure of ibuprofen.

acetaminophen, are highly effective for postoperative pain control [2]. Combining ibuprofen 200 mg with acetaminophen 500 mg has a significantly greater analgesic effect than an opioid medication such as oxycodone 15 mg with acetaminophen [2]. Thus, it may be appropriate to use opioids only for severe or refractory pain [2].

There may be a misconception that NSAIDs have an unacceptable risk of bleeding. Nonetheless, the bleeding risk profile of OTC IBU and the prescription strength (600 - 800 mg) is not well defined. That is, with the OTC use of IBU, there are few controlled studies regarding the anticoagulation effect of OTC use in the general population [1] [2].

Gastrointestinal bleeding can occur with OTC IBU use. IBU inhibits COX-1 and induces a reduction of gastric prostaglandins, which in turn reduces gastric protective mucus production, thus directly exposing the underlying cells to low pH gastric acid and enzymes such as pepsin [1] [2].

The GI-bleeding complication hospitalization rate for OTC-comparable doses of IBU is less than 0.2% [1]. With increasing age and concomitant medication use, the incidence of bleeding events does increase [1]. Nonetheless, there has been no consistent IBU dose-anticoagulation response relationship elucidated. This may mean that patients are poor historians when describing their side effects, or there are genetic metabolic differences that produce different outcomes, along with other potential reasons [7]. It is agreed that there appears to be a low incidence of bleeding events with OTC IBU.

OTC drugs for pain control are intended for short-term use and should not be taken for analgesia for more than 10 days. Longer use increases possible side effects. To avoid gastric side effects, IBU should be taken with food. Increased age, anemia, smoking, carcinoma, alcohol use, liver disease, frailty, anticoagulants, and selective serotonin reuptake inhibitors (SSRIs) are comorbidities that may increase the risk for gastric side effects [2] [4] [5] [8]-[11].

2. Methodology

A PubMed search was done using the terms ibuprofen, ibuprofen AND anticoagulant, ibuprofen AND drug interactions, and ibuprofen AND complications. No other search engine was used. Articles published between 1998 and 2024 were collected. Only articles addressing interactions with anticoagulants were considered; all others were excluded. The articles retrieved were assessed for relevance, and those deemed relevant are included herein. No human or animal subjects were used whatsoever in this work.

3. Pharmacodynamics of Ibuprofen

IBU inhibits the cyclooxygenase-1 and -2 (COX-1 and COX-2) enzymes. Inhibition of COX-1 affects the prostaglandin-induced protection of the gastrointestinal tract, and this action is well understood [10]. Nonetheless, various isoforms of IBU can cause varying degrees of gastric damage [12]. Selective COX-2 inhibitors are known to induce less gastric damage [12]. COX-2 leads to the production of prostaglandin E2 (PGE2), which produces redness, pain, and swelling; inhibition of COX-2 produces analgesia [5]. Prostaglandins are converted to thromboxane A_2 (TxA2) by COX-1 enzymes [5] [13]. TxA2 stimulates platelet aggregation for blood clotting. Thus, COX enzymes are inhibited, and then ultimately TxA2 production is reduced, along with platelet aggregation and coagulation [12] [14] [15].

4. Coagulation

Blood coagulation or thrombosis is the biological action in which liquid blood is converted to a gel or a clot. Coagulation involves platelets and vascular protein factors [16] (**Figure 2**). When vascular subendothelial collagen is damaged and exposed to platelets, coagulation begins. Platelets bind directly to the subendothelial collagen to form a plug to occlude the injury. Platelets release stored granules of several clotting factors that then bind fibrinogen. The fibrinogen crosslinks to a glycoprotein and aggregates more platelets, completing initial hemostasis [17]. Factor VII then induces fibrin formation to strengthen the platelet plug.

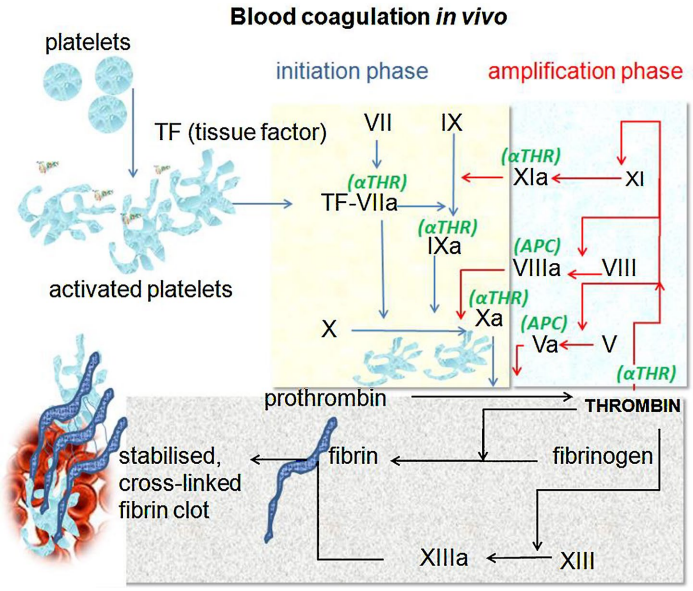

Figure 2. Schematic of the coagulation cascade.

The second stage of coagulation has two pathways that are artificially named: 1) extrinsic or tissue factor and 2) intrinsic or contact activation pathways. Both pathways play a role in fibrin formation to seal off bleeding or leaking blood vessels.

The extrinsic or tissue factor pathway is the more important. This pathway is a

cascade of enzymatic reactions involving coagulation factors. The main role of the extrinsic pathway is the rapid release of thrombin [18].

The intrinsic pathway is a cascade of reactions that aid clot formation, but its main role appears to be in inflammation and immunity [18] [19]. A therapeutic blockage of the intrinsic pathway does not increase the risk of significant bleeding but can contribute to the prevention of thrombosis [19].

In the end, the extrinsic and intrinsic pathways both end in a final common interactive pathway of factor X, thrombin, and fibrin.

Coagulation is a complex physiological series of chemical and enzymatic reactions that are activated and inhibited by a wide variety of enzymes and chemicals. In the end, without interference, a thrombus forms and bleeding ceases [18]-[20].

5. Ibuprofen and Coagulation

IBU has the lowest risk for gastrointestinal bleeding and platelet inactivation of all NSAIDs [21]. A single preoperative dose of 400 mg of IBU does not have a significantly increased occurrence of intraoperative or postoperative bleeding [22]-[24].

To reduce the risk of GI bleeding, IBU should not be taken for more than 10 days [25]. The lowest dose that produces the appropriate clinical effect is the dose that should be taken [26] [27].

Some studies report a low incidence of GI bleeding events with the use of 200-600 mg IBU for 10 days [1]. The gastrointestinal bleeding incidence among those using OTC-comparable doses ranged from 0 to 3.19 per 1000 patient years. The incidence of GI bleeding-related events increased with age and polypharmacy [1]. However, there was an inconsistent, statistically significant, ibuprofen dose-dependent anticoagulant response relationship. The relative risk of any GI bleeding-related events ranges from 1.1% to 2.4% for users of 200 - 600 mg IBU doses for 10 days when compared to non-users [1].

There are few published studies that have specifically investigated OTC IBU use [1]. Unfortunately, the large variety of methodologies, exposures, and outcomes precludes a direct comparison of many studies by means of a meta-analysis [1]. The various outcomes may imply that there are human differences in IBU metabolism [1]. Thus, patients with susceptible phenotypes that affect IBU metabolism may react with varying degrees of gastrointestinal bleeding severity [28].

6. Ibuprofen Interaction with Anticoagulant, Anti-Platelet, and Direct Anti-Thrombotic Agents

Anticoagulants inhibit clot formation. There are many available with various mechanisms of action. Since IBU acts to inhibit platelet aggregation, there may be an increased clinical anticoagulation effect when co-administered with other anticoagulants, antithrombotic, or antiplatelet agents [28] [29].

6.1. Ibuprofen and Warfarin

In one study, the effect of IBU anticoagulation interaction with warfarin on he-

mostasis was tested in 20 patients taking warfarin for venous thromboembolism [27]. IBU 600 mg taken three times per day orally was tested for 1 week [30]. Bleeding time, prothrombin time, platelet count, and urinalysis for hemoglobin were observed. These tests were performed just before, 90 minutes after the first dose of IBU, and after a one-week duration of treatment. Bleeding time was significantly prolonged after 90 minutes following a single IBU 600 mg dose, and after 1 week. Hematuria and hematoma were seen in all cases following week-long co-administration. It was concluded that ibuprofen can cause significant anticoagulation issues in patients being treated with concurrent warfarin after one week [30]. Thus, older patients under anticoagulant and polypharmacy therapy may be at increased risk for bleeding complications [30]-[34].

Warfarin (Coumadin®) acts by blocking the enzymatic reduction of vitamin K. Vitamin K is an important cofactor in the synthesis of clotting Factors II (prothrombin), VII, IX, and X. It can take 3 - 5 days for warfarin to have its full therapeutic effect due to the pre-treatment reservoir of Factors II, VII, IX, and X [30] [34].

IBU causes an increase in the INR in these warfarin patients by an additive effect [35] [36]. IBU 600 mg taken orally three times a day for 7 days can cause an increase in the INR of patients taking warfarin [35] [36]; however, there may not be a significant effect on platelet count and prothrombin time. Therefore, the increase in anticoagulation in most patients may remain within normal limits. Nonetheless, microscopic hematuria and hematoma can occur in these patients. These sequelae may be problematic in elderly polypharmacy patients [33] [34]. Thus, if IBU is to be administered for an extended period in these patients, the dental clinician should consult with the patient's physician, who should monitor the warfarin INR before and during concurrent IBU-warfarin therapy. If the INR is prolonged beyond the intended clinical range, the IBU treatment should be discontinued [36] [37].

Much of the work on the IBU-warfarin interaction was done on rats. Rats are much more sensitive to this interaction than humans; nonetheless, extrapolation to human clinical usage may not be appropriate [36] [37].

6.2. Ibuprofen and Aspirin

The anti-platelet agent aspirin (ASA, acetyl salicylic acid) is a non-selective COX inhibitor NSAID. A single dose of ASA inhibits platelet function for 48 hours and inhibits platelet aggregation for the life of the platelet [32] [33]. Short-term usage of IBU slightly reduces platelet aggregation as compared to aspirin [25] [26] [32] [35] [36]. The action of ASA occurs at different loci in the coagulation cascade than IBU. Nonetheless, IBU does interfere with the antiplatelet effect of aspirin (ASA), and this makes the ASA less effective for cardioprotection and stroke prevention [32] [33]. IBU can inhibit low-dose ASA's ability to reduce the antiplatelet effect [31] [32]. This problem can be avoided by waiting 30 - 120 minutes after the ASA dose to administer the IBU or administering the IBU dose 6 - 8 hours prior to the ASA dose [32] [34] [35]. However, due to the delayed absorption of enteric-

coated ASA, this time frame may not apply. Another study suggested that IBU may be taken with a 30- to 60-minute hiatus before or after ASA oral administration to prevent an interaction [31] [32]. However, if IBU is taken only as an occasional single dose or for a short term, then there is minimal disruption of the ASA cardiovascular protective action [32] [34].

Recent reports have minimized the therapeutic effect of ASA [38]. Since ASA and IBU are NSAIDs, this may mean that the effects of these agents are uncertain, as well as their interaction. Further investigation needs to be done to elucidate the therapeutics and interactions.

6.3. Ibuprofen and Direct-Acting Antithrombotics

The direct-acting antithrombotics (DAA) (non-vitamin K antagonists) act by inhibiting elements of the coagulation cascade, factor Xa and IIa [39] [40]. Dabigatran (Pradaxa®) is a direct thrombin inhibitor, and rivaroxaban (Xarelto®) and apixaban (Eliquis®) are direct Factor Xa inhibitors [40]. These commonly prescribed anticoagulants do not require routine monitoring [41]. While this is an advantage, the patient has less contact with the prescriber and may not be mindful of the potential for interactions with OTC medications [41]. Nonetheless, the incidence of serious interactions with IBU is low when OTC guidelines are followed, 200 mg every 4 - 6 hours for less than 10 days [42]. Nonetheless, IBU can increase the incidence of bleeding in patients taking apixaban (Eliquis), rivaroxaban (Xarelto), or dabigatran (Pradaxa) by an additive effect [40]. Thus, co-administration of IBU with these medications should be avoided.

6.4. Considerations

Table 1 provides a list of considerations before prescribing IBU (**Table 1**) [43]. If IBU must be prescribed, then close monitoring of the patient's compliance and coagulation status should be conducted [43]-[46].

Ibuprofen interactions can be influenced by a variety of individual patient factors. A patient of advanced age may have reduced renal function and altered drug metabolic activity, which increases the risk for gastrointestinal bleeding and renal impairment. An aged patient with hypertension may be susceptible to renal dysfunction. A patient with a history of GI bleeding is at risk for a recurrence. A patient with renal impairment may not have adequate renal clearance of IBU, which leads to an increased plasma level and risk for toxicity. A polypharmacy patient, especially one taking anticoagulants, has an elevated risk for GI bleeding. Patients with a history of cardiovascular disease have an increased risk of hypertension and heart failure if they take ibuprofen. A patient with an allergy to NSAIDs has a high risk for hypersensitivity or an anaphylactic reaction to ibuprofen. Individual patient factors highlight the need for careful assessment and monitoring when prescribing ibuprofen to mitigate these risks [46] [47].

The findings regarding ibuprofen interactions, particularly concerning cardiovascular and gastrointestinal risks, are significant. There are important issues

Table 1. Considerations for ibuprofen use.

No.	Considerations
1	Assessment of indications.
2	Is there an alternative medication?
3	Is a referral indicated?
4	Bleeding risk assessment.
5	Medical history: age, previous bleeding, gastric disorders, malignancies, alcoholism, coagulopathy, and more.
6	Medication history: cardiac issues, direct anticoagulants, warfarin, antiplatelets, herbals, testosterone, renal dysfunction, and others.
7	Thrombotic risk assessment: stroke, deep vein thrombosis, smoking, obesity, immobility, impending surgery, hypercoagulable state, and more.
8	Risk-benefit assessment.
9	Avoid ibuprofen with warfarin and direct anticoagulants.
10	Close monitoring of the patient may be required.

Adapted from: [44].

about whether interactions are a class effect among all nonsteroidal anti-inflammatory drugs (NSAIDs). IBU is a non-selective NSAID and has associations with increased cardiovascular events and GI complications. The risks are different when compared to COX-2 selective inhibitors like celecoxib [48]-[50].

IBU and naproxen inhibit both COX-1 and COX-2 enzymes for effective pain relief. Nonetheless, they can induce GI bleeding. COX-1 has a protective role for the gastric mucosa. Yet, COX-2 inhibitors selectively inhibit the COX-2 inflammation enzyme and have a reduced risk for GI bleeding. Additionally, COX-2 inhibitors do not mitigate the pro-thrombotic effects of COX-1 inhibition [47]-[50].

IBU interactions can pose significant risks, but these may not apply to all NSAIDs.

IBU interacts with a variety of medications, such as anticoagulants, and can influence renal function.

Function and cardiovascular risk. However, these interactions do not represent a class effect for all NSAIDs. The risk and severity of interactions can be different among NSAIDs because of varied pharmacological properties, dosage, and duration of use [47]-[50].

IBU inhibits both COX-1 and COX-2 enzymes, which can lead to GI issues and cardiovascular events if there is prolonged usage. There would be inhibition of COX-1 protective gastric and renal mechanisms. Celecoxib, a COX-2 selective inhibitor, reduces inflammation and has a lower risk of GI side effects. Nonetheless, it has a risk for cardiovascular events in some patients.

There are overlapping risks, and specific interactions and side effects can vary significantly. Thus, it is important to assess each patient and use clinical discretion when prescribing these medications [47]-[50].

7. Conclusions

Current information shows that IBU affects coagulation by mildly inhibiting platelet aggregation when taken for less than 10 days. IBU 400 mg every 6 hours taken for less than 48 hours is unlikely to induce an adverse bleeding event in patients taking anticoagulants. However, after 10 days of daily dosing, there may be an increased risk for bleeding.

Most patients have poor compliance, and if IBU is to be administered, the clinician should be certain that the patient understands the implications of IBU dosing and potential drug interactions.

Investigations of these interactions are needed to provide the clinician with appropriate prescribing protocols.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

References

[1] Michels, S.L., Collins, J., Reynolds, M.W., Abramsky, S., Paredes-Diaz, A. and McCarberg, B. (2012) Over-the-Counter Ibuprofen and Risk of Gastrointestinal Bleeding Complications: A Systematic Literature Review. *Current Medical Research and Opinion*, **28**, 89-99. https://doi.org/10.1185/03007995.2011.633990

[2] Cramer, J.D., Barnett, M.L., Anne, S., Bateman, B.T., Rosenfeld, R.M., Tunkel, D.E., *et al.* (2020) Nonopioid, Multimodal Analgesia as First-Line Therapy after Otolaryngology Operations: Primer on Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). *Otolaryngology-Head and Neck Surgery*, **164**, 712-719. https://doi.org/10.1177/0194599820947013

[3] Bailey, E., Worthington, H.V., van Wijk, A., Yates, J.M., Coulthard, P. and Afzal, Z. (2013) Ibuprofen and/or Paracetamol (Acetaminophen) for Pain Relief after Surgical Removal of Lower Wisdom Teeth. *Cochrane Database of Systematic Reviews*, **2013**, CD004624. https://doi.org/10.1002/14651858.cd004624.pub2

[4] Grosser, T., Ricciotti, E. and FitzGerald, G.A. (2017) The Cardiovascular Pharmacology of Nonsteroidal Anti-Inflammatory Drugs. *Trends in Pharmacological Sciences*, **38**, 733-748. https://doi.org/10.1016/j.tips.2017.05.008

[5] Davies, N.M. (1998) Clinical Pharmacokinetics of Ibuprofen. The First 30 Years. *Clinical Pharmacokinetics*, **34**, 101-154. https://doi.org/10.2165/00003088-199834020-00002

[6] British National Formulary (2014) Ibuprofen on Both. British Medical Association, 686-688.

[7] Tschopp, M. and Reinhart, W.H. (2008) Platelet Aggregation under High Shear Conditions during and after a 28-Day Administration of 100 mg Acetylsalicylic Acid in Healthy Volunteers. *Clinical Hemorheology and Microcirculation*, **38**, 45-50.

[8] Nakamura, N., Kaida, D., Tomita, Y., Miyata, T., Miyashita, T., Fujita, H., *et al.* (2021) Risk Factors for Overall Complications and Remote Infection after Gastrectomy in Elderly Gastric Cancer Patients. *In Vivo*, **35**, 2917-2921. https://doi.org/10.21873/invivo.12582

[9] Gong, Y., Zhang, Y.M., Zhu, J.Q., He, S., Dou, L.Z., *et al.* (2021) Analysis of Risk Factors for Delayed Bleeding after Endoscopic Submucosal Dissection of Gastric Ep-

ithelial Neoplasm. *Chinese Journal of Oncology*, **43**, 861-865.

[10] Enderes, J., Teschke, J., von Websky, M., Manekeller, S., Kalff, J.C. and Glowka, T.R. (2021) Active Smokers Show Ameliorated Delayed Gastric Emptying after Pancreatoduodenectomy. *BMC Surgery*, **21**, Article No. 316. https://doi.org/10.1186/s12893-021-01311-2

[11] Fouquet, G., Coman, T., Hermine, O. and Côté, F. (2019) Serotonin, Hematopoiesis and Stem Cells. *Pharmacological Research*, **140**, 67-74. https://doi.org/10.1016/j.phrs.2018.08.005

[12] Kakuta, H., Zheng, X., Oda, H., Harada, S., Sugimoto, Y., Sasaki, K., *et al.* (2008) Cyclooxygenase-1-Selective Inhibitors Are Attractive Candidates for Analgesics That Do Not Cause Gastric Damage. Design and *in Vitro*/*in Vivo* Evaluation of a Benzamide-Type Cyclooxygenase-1 Selective Inhibitor. *Journal of Medicinal Chemistry*, **51**, 2400-2411. https://doi.org/10.1021/jm701191z

[13] Chen, H. (2018) Role of Thromboxane A2 Signaling in Endothelium-Dependent Contractions of Arteries. *Prostaglandins & Other Lipid Mediators*, **134**, 32-37. https://doi.org/10.1016/j.prostaglandins.2017.11.004

[14] Rainsford, K.D. (2012) Relation of Analgesic Effects to COX-1 and COX-2 Inhibition (3.3). In: *Ibuprofen*: *Pharmacology*, *Therapeutics and Side Effects*, Springer, 49-57.

[15] Rao, P. and Knaus, E.E. (2008) Evolution of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs): Cyclooxygenase (COX) Inhibition and Beyond. *Journal of Pharmacy & Pharmaceutical Sciences*, **11**, 81-110. https://doi.org/10.18433/j3t886

[16] Furie, B. and Furie, B.C. (2005) Thrombus Formation *in Vivo*. *Journal of Clinical Investigation*, **115**, 3355-3362. https://doi.org/10.1172/jci26987

[17] Pallister, C.J. and Watson, M.S. (2010) Blood Coagulation: Mechanisms. In: *Haematology*, Scion Publishing, 334-336.

[18] Mackman, N., Tilley, R.E. and Key, N.S. (2007) Role of the Extrinsic Pathway of Blood Coagulation in Hemostasis and Thrombosis. *Arteriosclerosis*, *Thrombosis*, *and Vascular Biology*, **27**, 1687-1693. https://doi.org/10.1161/atvbaha.107.141911

[19] Long, A.T., Kenne, E., Jung, R., Fuchs, T.A. and Renné, T. (2015) Contact System Revisited: An Interface between Inflammation, Coagulation, and Innate Immunity. *Journal of Thrombosis and Haemostasis*, **14**, 427-437. https://doi.org/10.1111/jth.13235

[20] Hoffbrand, A.V. (2002) Platelets, Blood Coagulation and Haemostasis. In: *Essential Haematology*, Wiley-Blackwell, 314-329.

[21] Hersh, E.V., Moore, P.A. and Ross, G.L. (2000) Over-the-Counter Analgesics and Antipyretics: A Critical Assessment. *Clinical Therapeutics*, **22**, 500-548. https://doi.org/10.1016/s0149-2918(00)80043-0

[22] Dionne, R.A. and Cooper, S.A. (1978) Evaluation of Preoperative Ibuprofen for Postoperative Pain after Removal of Third Molars. *Oral Surgery*, *Oral Medicine*, *Oral Pathology*, **45**, 851-856. https://doi.org/10.1016/s0030-4220(78)80004-8

[23] Dionne, R.A., Campbell, R.A., Cooper, S.A., Hall, D.L. and Buckingham, B. (1983) Suppression of Postoperative Pain by Preoperative Administration of Ibuprofen in Comparison to Placebo, Acetaminophen, and Acetaminophen Plus Codeine. *The Journal of Clinical Pharmacology*, **23**, 37-43. https://doi.org/10.1002/j.1552-4604.1983.tb02702.x

[24] Dionne, R.A. (1986) Suppression of Dental Pain by the Preoperative Administration of Flurbiprofen. *The American Journal of Medicine*, **80**, 41-49. https://doi.org/10.1016/0002-9343(86)90110-5

[25] Stichtenoth, D.O., Tsikas, D., Gutzki, F.M. and Frölich, J.C. (1996) Effects of Ketoprofen and Ibuprofen on Platelet Aggregation and Prostanoid Formation in Man. *European Journal of Clinical Pharmacology*, **51**, 231-234. https://doi.org/10.1007/s002280050189

[26] Jackson, D.L., Moore, P.A. and Hargreaves, K.M. (1989) Preoperative Nonsteroidal Anti-Inflammatory Medication for the Prevention of Postoperative Dental Pain. *The Journal of the American Dental Association*, **119**, 641-647. https://doi.org/10.1016/s0002-8177(89)95018-6

[27] Wynn, R.L., Meiller, T.F. and Crossley, H.L. (2013) Drug Information Handbook for Dentistry. Lexi-Comp Inc, 711-715.

[28] Martini, W.Z., Rodriguez, C.M., Deguzman, R., Guerra, J.B., Martin, A.K., Pusateri, A.E., *et al.* (2016) Dose Responses of Ibuprofen *in Vitro* on Platelet Aggregation and Coagulation in Human and Pig Blood Samples. *Military Medicine*, **181**, 111-116. https://doi.org/10.7205/milmed-d-15-00381

[29] McElwee, N.E., Veltri, J.C., Bradford, D.C. and Rollins, D.E. (1990) A Prospective, Population-Based Study of Acute Ibuprofen Overdose: Complications Are Rare and Routine Serum Levels Not Warranted. *Annals of Emergency Medicine*, **19**, 657-662. https://doi.org/10.1016/s0196-0644(05)82471-0

[30] Schulman, S. and Henriksson, K. (1989) Interaction of Ibuprofen and Warfarin on Primary Haemostasis. *Rheumatology*, **28**, 46-49. https://doi.org/10.1093/rheumatology/28.1.46

[31] U.S. Food and Drug Administration (2006) Information for Healthcare Professionals: Concomitant Use of Ibuprofen and Aspirin.

[32] Shibata, K., Akagi, Y., Nozawa, N., Shimomura, H. and Aoyama, T. (2017) Influence of Nonsteroidal Anti-Inflammatory Drugs on Aspirin's Antiplatelet Effects and Suggestion of the Most Suitable Time for Administration of Both Agents without Resulting in Interaction. *Journal of Pharmaceutical Health Care and Sciences*, **3**, Article No. 9. https://doi.org/10.1186/s40780-017-0078-7

[33] Ageno, W., Gallus, A.S., Wittkowsky, A., Crowther, M., *et al.* (2012) Oral Anticoagulant Therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*, **141**, e44S-e88S.

[34] Gulløv, A.L., Koefoed, B.G. and Petersen, P. (1999) Bleeding during Warfarin and Aspirin Therapy in Patients with Atrial Fibrillation: The AFASAK 2 Study. Atrial Fibrillation Aspirin and Anticoagulation. *Archives of Internal Medicine*, **159**, 1322-1328.

[35] Garcia, D.A., Regan, S., Henault, L.E., Upadhyay, A., *et al.* (2008) Risk of Thromboembolism with Short-Term Interruption of Warfarin Therapy. *Archives of Internal Medicine*, **168**, 63-69. https://doi.org/10.1001/archinternmed.2007.23

[36] Sancilio, L.F., Taylor, M.A., Mathur, P.P. and Crowe, J.T. (1985) Interaction between Warfarin and Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) in Rats. *Life Sciences*, **36**, 1041-1050. https://doi.org/10.1016/0024-3205(85)90489-8

[37] Dentali, F., Douketis, J.D., Woods, K., Thabane, L., Foster, G., Holbrook, A., *et al.* (2006) Does Celecoxib Potentiate the Anticoagulant Effect of Warfarin? A Randomized, Double-Blind, Controlled Trial. *Annals of Pharmacotherapy*, **40**, 1241-1247. https://doi.org/10.1345/aph.1g733

[38] Tai, W.A. (2022) Stroke: Primary Prevention. *FP Essent*, **512**, 11-17.

[39] Peacock, W.F., Rafique, Z. and Singer, A.J. (2016) Direct-Acting Oral Anticoagulants:

Practical Considerations for Emergency Medicine Physicians. *Emergency Medicine International*, **2016**, 1-13. https://doi.org/10.1155/2016/1781684

[40] Bassand, J.P. (2014) Novel Oral Anticoagulants in Acute Coronary Syndrome: Re-Evaluating the Thrombin Hypothesis. *EuroIntervention*, **9**, 1333-1341. https://doi.org/10.4244/eijv9i11a224

[41] Tarn, D.M., Barrientos, M., Wang, A.Y., Ramaprasad, A., Fang, M.C. and Schwartz, J.B. (2020) Prevalence and Knowledge of Potential Interactions between Over-the-Counter Products and Apixaban. *Journal of the American Geriatrics Society*, **68**, 155-162. https://doi.org/10.1111/jgs.16193

[42] Hersh, E.V., Pinto, A. and Moore, P.A. (2007) Adverse Drug Interactions Involving Common Prescription and Over-the-Counter Analgesic Agents. *Clinical Therapeutics*, **29**, 2477-2497. https://doi.org/10.1016/j.clinthera.2007.12.003

[43] Lu, Y., Shen, D., Pietsch, M., Nagar, C., Fadli, Z., Huang, H., *et al.* (2015) A Novel Algorithm for Analyzing Drug-Drug Interactions from MEDLINE Literature. *Scientific Reports*, **5**, Article No. 17357. https://doi.org/10.1038/srep17357

[44] Kent, A.P. (2020) Navigating NSAID Use in Patients Receiving Oral Anticoagulation: Is There a Safe Course? *Thrombosis and Haemostasis*, **120**, 1001-1003. https://doi.org/10.1055/s-0040-1713098

[45] Frazee, L.A. and Reed, M.D. (1995) Warfarin and Nonsteroidal Anti-Inflammatory Drugs: Why Not? *Annals of Pharmacotherapy*, **29**, 1289-1291. https://doi.org/10.1177/106002809502901218

[46] Davidson, B.L., Verheijen, S., Lensing, A.W.A., Gebel, M., Brighton, T.A., Lyons, R.M., *et al.* (2014) Bleeding Risk of Patients with Acute Venous Thromboembolism Taking Nonsteroidal Anti-Inflammatory Drugs or Aspirin. *JAMA Internal Medicine*, **174**, 947-953. https://doi.org/10.1001/jamainternmed.2014.946

[47] Ghosh, S., Lahens, N., Barekat, K., Tang, S.Y., *et al.* (2024) Metabolomic Response to Non-Steroidal Anti-Inflammatory Drugs.

[48] Lai, J.H., Chang, L., Lin, S., Mo, S., Liu, H. and Qin, J. (2026) Letter to the Editor: "Incidence of Kidney Toxicity of Non-Steroidal Anti-Inflammatory Drugs in Critically Ill Patients". *Journal of Critical Care*, **91**, Article 155319. https://doi.org/10.1016/j.jcrc.2025.155319

[49] Abdallah, N.A., Elmansi, H., Alossaimi, M.A., Altamimi, A.S.A., El Abass, S.A. and Elama, H.S. (2026) Harmonizing Drug Analysis and Sustainability: Spectroscopic Quantification of Antiplatelet-Anticoagulant Regimens. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, **345**, Article 126769. https://doi.org/10.1016/j.saa.2025.126769

[50] Petersen, S.R., Bonnesen, K., Larsen, J.B., Pedersen, L. and Schmidt, M. (2025) Bleeding Risk Using Non-Steroidal Anti-Inflammatory Drugs in Anticoagulated Patients with Atrial Fibrillation: A Nationwide Cohort Study. *European Heart Journal—Quality of Care and Clinical Outcomes*, **11**, 1340-1350. https://doi.org/10.1093/ehjqcco/qcaf076