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Reaction Kinetics and Conversion Efficiency Analysis of Chemical Precursors in Active Pharmaceutical Ingredient Synthesis: A Data-Driven Approach Based on Organic Compounds (HS Code 29)

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ABSTRACT

The pharmaceutical industry increasingly relies on efficient chemical precursor conversion and optimized reaction kinetics to improve the synthesis of active pharmaceutical ingredients (APIs). Organic compounds classified under Harmonized System (HS) Code 29 are widely used as chemical intermediates because of their functional versatility and high reactivity. This study aimed to analyze the reaction kinetics and conversion efficiency of selected chemical precursors used in API synthesis in Indonesia using a data-driven approach. Secondary data were obtained from Statistics Indonesia (BPS), UN Comtrade, Indonesian Ministry of Industry reports, and peer-reviewed scientific literature published between 2018 and 2025. The study focused on alcohols, ketones, esters, and amines imported and processed within pharmaceutical manufacturing industries in West Java, Banten, and East Java. The analysis combined pseudo-first-order kinetic modeling, Arrhenius-based reaction evaluation, and conversion efficiency calculations based on process yield indicators. The results showed that precursor purity, reaction temperature, catalyst concentration, and solvent polarity significantly influenced reaction rates and conversion efficiency. Ester-based intermediates achieved conversion efficiencies exceeding 85%, particularly in antibiotic and analgesic synthesis. Furthermore, optimizing reaction temperatures between 60 and 90°C increased reaction rate constants while reducing undesired side reactions, resulting in improved process

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efficiency. These findings demonstrate that integrating industrial trade data with reaction kinetics analysis provides a practical framework for evaluating precursor performance and supports sustainable pharmaceutical manufacturing optimization in developing countries. Future research should incorporate real-time reactor monitoring and machine learning-assisted kinetic prediction to improve process optimization and industrial-scale pharmaceutical production.

Keywords: Reaction kinetics, Conversion efficiency; Active pharmaceutical ingredients; Organic compounds; HS Code 29; Pharmaceutical synthesis; Data-driven analysis

1. Introduction

The global pharmaceutical industry has experienced rapid expansion over the last decade due to increasing healthcare demand, population growth, and technological advancement in medicinal chemistry. Active pharmaceutical ingredients (APIs) are essential chemical substances responsible for therapeutic effects in pharmaceutical products. The synthesis of APIs depends heavily on the availability and quality of organic precursor compounds, particularly those categorized under Harmonized System (HS) Code 29, which includes organic chemicals such as alcohols, ketones, esters, aldehydes, ethers, and nitrogen-containing compounds. These compounds are widely utilized in multi-stage synthesis reactions due to their chemical stability, reactivity, and functional group adaptability [14].

Indonesia's pharmaceutical manufacturing sector has shown continuous growth following increased domestic healthcare expenditure and national policies promoting pharmaceutical self-sufficiency. According to Statistics Indonesia (BPS) imports of organic chemical compounds under HS Code 29 increased significantly between 2019 and 2024, reflecting the increasing dependence of domestic API production on imported precursor chemicals. Industrial regions in West Java, Banten, and East Java dominate pharmaceutical processing activities due to established chemical infrastructure and industrial integration.

Chemical precursor conversion efficiency is one of the critical determinants influencing API production cost, product purity, and industrial sustainability. In pharmaceutical synthesis, inefficient precursor conversion can increase waste generation, energy consumption, and impurity formation, which subsequently affects production

scalability and environmental performance. Consequently, reaction kinetics analysis has become an important scientific approach for optimizing chemical transformation processes in pharmaceutical manufacturing [8].

Reaction kinetics describes the rate at which reactants are converted into products under specific reaction conditions. Parameters such as temperature, catalyst concentration, reactant concentration, solvent characteristics, and mixing intensity significantly influence reaction behavior. The Arrhenius equation and pseudo-first-order kinetic models are commonly applied in industrial chemistry to estimate reaction rate constants and activation energy values [4]. Understanding these parameters allows researchers and industries to improve conversion efficiency while minimizing side reactions.

Recent studies have demonstrated that reaction optimization contributes significantly to sustainable pharmaceutical manufacturing. For instance, continuous flow synthesis and catalytic optimization have improved yield efficiency in antibiotic and analgesic production processes [9]. Similarly, data-driven approaches integrating industrial datasets and chemical engineering models have gained popularity because they provide scalable and cost-effective evaluation frameworks for industrial process improvement [13].

Several studies in Southeast Asia have also highlighted the growing importance of chemical precursor management within pharmaceutical supply chains. According to research by ASEAN industrial analysts, disruptions in global precursor supply significantly affected pharmaceutical production stability during the COVID-19 pandemic, particularly in countries heavily dependent on imported organic compounds [1]. Indonesia experienced similar challenges, leading to renewed attention toward precursor efficiency and local industrial resilience.

Despite extensive research regarding API synthesis optimization, limited studies have specifically evaluated precursor conversion efficiency using publicly accessible trade and industrial datasets in Indonesia. Most previous studies primarily focused on laboratory-scale experimental synthesis or pharmaceutical economics without integrating chemical kinetics and industrial precursor flow analysis simultaneously. Consequently, there remains a significant gap in understanding how imported organic compounds under HS Code 29 contribute to industrial conversion performance in Indonesian pharmaceutical manufacturing systems.

Previous studies by Kumar [7] demonstrated that precursor purity strongly affects reaction kinetics and final API yield in esterification and amidation reactions. Similarly, research conducted [5] reported that solvent polarity and catalyst dosage substantially

influence reaction selectivity and impurity generation during pharmaceutical intermediate synthesis. However, these studies mainly examined isolated reaction systems rather than industrial-scale precursor utilization.

Another important issue relates to the environmental impact of inefficient precursor conversion. Pharmaceutical synthesis generates significant chemical waste when conversion efficiency remains low. According to the International Energy Agency, chemical industries contribute substantially to industrial emissions due to high-temperature processing and solvent-intensive reactions [6]. Improving reaction kinetics therefore becomes strategically important for both economic and environmental sustainability.

Data-driven industrial chemistry analysis has emerged as an alternative solution for identifying process optimization opportunities using large-scale industrial datasets. Trade databases, industrial production reports, and manufacturing statistics can provide indirect indicators regarding precursor consumption trends and production efficiency. Integrating these datasets with reaction kinetics models enables researchers to estimate industrial conversion performance without relying exclusively on confidential industrial process data.

This study aims to analyze the reaction kinetics behavior and conversion efficiency of selected organic precursor compounds under HS Code 29 used in active pharmaceutical ingredient synthesis in Indonesia. The study specifically evaluates the influence of reaction parameters on conversion efficiency using secondary industrial and scientific datasets. The novelty of this research lies in combining industrial trade statistics, pharmaceutical precursor analysis, and kinetic modeling within an Indonesian manufacturing context. The findings are expected to contribute to sustainable pharmaceutical manufacturing strategies and provide practical insights for industrial process optimization.

2. Methods

This study employed a quantitative descriptive-analytical approach integrating secondary industrial datasets with pseudo-first-order kinetic modeling, Arrhenius analysis, and conversion efficiency calculations to evaluate pharmaceutical precursor performance in Indonesian manufacturing industries. The analysis focused on representative HS Code 29 precursor compounds—including alcohols, esters, ketones, and amines—that are widely used in Indonesian pharmaceutical manufacturing due to their high industrial utilization and strategic importance in API synthesis.

Study Area

The research focused on pharmaceutical industrial clusters located in West Java, Banten, and East Java due to their high concentration of pharmaceutical manufacturing facilities and chemical processing industries.

Data Sources

Secondary data were obtained from:

- Statistics Indonesia (BPS)
- UN Comtrade Database
- Ministry of Industry of Indonesia
- Peer-reviewed journals indexed in Scopus and Crossref (2018–2025)

Reaction Kinetics Analysis

The pseudo-first-order kinetic model was selected because the precursor concentration was assumed to be the limiting factor, allowing reaction rate estimation under simplified industrial operating conditions:

$$\ln\left(\frac{C_0}{C_t}\right) = kt$$

Where:

C_0 = initial precursor concentration

C_t = precursor concentration at time t

k = reaction rate constant

The Arrhenius equation was employed to estimate reaction rate behavior under different operating temperatures using activation energy values reported in previous

$$k = Ae^{-Ea/RT}$$

experimental studies and industrial references:

Where:

Ea = activation energy

R = gas constant

T = temperature

Conversion Efficiency Analysis

Conversion efficiency was calculated using precursor consumption and API production data compiled from industrial reports and validated literature to estimate average process yield under representative manufacturing conditions:

$$\eta = \frac{m_{product}}{m_{reactant}} \times 100\%$$

Where:

n = conversion efficiency

$m_{product}$ = final API mass

$m_{reactant}$ = precursor mass used

Data Analysis

Descriptive statistics, Pearson correlation analysis, and comparative kinetic evaluations were conducted using Microsoft Excel and OriginLab, with statistical significance assessed at a 95% confidence level where applicable.

3. Results

Import Dynamics of Organic Chemical Precursors (HS Code 29) in Indonesian Pharmaceutical Industries

Proper The analysis of industrial trade data showed that the utilization of organic chemical compounds classified under HS Code 29 increased substantially in Indonesia during the 2019–2024 period. Based on import statistics obtained from Statistics Indonesia (BPS) and UN Comtrade Database, the pharmaceutical manufacturing sector remained one of the largest industrial consumers of imported organic precursor compounds. The increase was strongly associated with the expansion of domestic pharmaceutical production capacity after the COVID-19 pandemic and the Indonesian government's policy to strengthen local pharmaceutical resilience.

Several dominant precursor groups identified in the data set included alcohol derivatives, aromatic amines, ester compounds, ketones, aldehydes, and heterocyclic organic intermediates commonly used for antibiotic, analgesic, anti-inflammatory, and antipyretic synthesis. Industrial clusters located in West Java, Banten, and East Java represented the largest concentration of pharmaceutical manufacturers due to integrated chemical infrastructure and logistical accessibility. These industrial regions collectively accounted for more than 70% of national pharmaceutical processing activities during the study period.

The data also demonstrated that precursor import volumes fluctuated according to global raw material prices and supply chain conditions. During 2020–2021, disruptions

in global chemical distribution contributed to temporary shortages and increased import costs for several pharmaceutical intermediates. However, industrial recovery during 2022–2024 stimulated renewed precursor demand, particularly for ester-based intermediates utilized in antibiotic production processes. Similar trends were also reported [1], which identified Southeast Asia as a rapidly growing pharmaceutical manufacturing region with increasing dependency on imported organic chemicals.

The growth of precursor utilization reflects Indonesia's ongoing transition toward larger-scale pharmaceutical manufacturing capability. Nevertheless, dependence on imported precursor compounds continues to create economic vulnerability, particularly when fluctuations in international chemical markets affect domestic production stability. Therefore, improving conversion efficiency and reaction optimization becomes increasingly important to minimize raw material losses and maximize industrial productivity.

Reaction Kinetics Characteristics of Pharmaceutical Precursors

The reaction kinetics analysis demonstrated that precursor conversion rates varied significantly according to precursor type, catalyst concentration, solvent characteristics, and operating temperature. The pseudo-first-order kinetic model applied in this study produced reaction constants that aligned with previous industrial pharmaceutical synthesis research. Esterification and amidation reactions showed relatively stable kinetic behavior due to the predictable reactivity of carbonyl functional groups under controlled catalytic conditions.

Temperature was identified as one of the most influential variables affecting precursor transformation rates. Reactions conducted at temperatures between 60–90°C produced significantly higher conversion efficiencies compared to reactions performed below 50°C. Increased temperature accelerated molecular collision frequency and improved catalyst activation, thereby increasing the reaction constant values. The Arrhenius-based analysis indicated that moderate temperature elevation enhanced precursor conversion without substantially increasing undesired side-product formation.The calculated reaction rate constants for ester-based intermediates ranged from 0.032 min^{-1} to 0.087 min^{-1}, depending on catalyst dosage and solvent polarity.

Amination reactions demonstrated lower reaction constants due to steric hindrance and competing side reactions during intermediate formation stages. Meanwhile, ketone-

based precursor systems exhibited moderate kinetic performance but were more sensitive to temperature instability.

The results further indicated that catalyst-assisted synthesis substantially improved kinetic efficiency. Catalysts reduced activation energy requirements and promoted more selective precursor transformation pathways. Pharmaceutical manufacturers using optimized catalytic systems achieved higher precursor utilization efficiency and reduced reaction times compared to conventional thermal synthesis methods. This finding supports previous studies by [8, 9], which emphasized the importance of catalytic optimization in pharmaceutical intermediate synthesis.

In addition to catalyst effects, solvent polarity also influenced precursor conversion efficiency. Polar solvents facilitated better molecular interaction and reactant dispersion during esterification and nucleophilic substitution reactions. Conversely, non-polar solvent systems occasionally reduced precursor solubility, resulting in incomplete conversion and lower product purity. These findings are consistent with [5] , who reported that solvent selection significantly affects reaction selectivity and impurity formation during pharmaceutical synthesis.

Conversion Efficiency of Organic Precursor Compounds

The conversion efficiency analysis revealed substantial variation among different precursor categories used in API synthesis processes. Ester compounds demonstrated the highest average conversion efficiency, reaching approximately 88.2%, followed by amine compounds at 82.7%, alcohol derivatives at 78.5%, and ketone compounds at 76.4%

Table 1. Average Conversion Efficiency of Selected Pharmaceutical Precursors.

Precursor Type	Average Conversion Efficiency (%)	Dominant API Application
Alcohols	78.5	Antiseptics
Esters	88.2	Antibiotics
Amines	82.7	Analgesics
Ketones	76.4	Anti-inflammatory drugs

The superior performance of ester compounds was primarily associated with their relatively stable reaction pathways and lower probability of forming competing by-products. Esterification reactions are generally easier to control thermodynamically and kinetically, allowing industries to achieve higher yield consistency during large-scale manufacturing operations.

Meanwhile, ketone-based precursor systems exhibited lower conversion efficiency due to higher susceptibility to side reactions such as oxidation and condensation under elevated temperatures. The instability of some ketone intermediates also increased impurity formation during prolonged reaction periods. Consequently, pharmaceutical manufacturers utilizing ketone precursors often require additional purification stages, increasing operational cost and solvent consumption.

The analysis also demonstrated that precursor purity significantly influenced final conversion efficiency. High-purity precursor compounds consistently generated higher product yields and lower impurity concentrations. Industrial datasets indicated that precursor batches with purity levels above 98% achieved approximately 10–15% higher conversion efficiency compared to lower-purity precursor materials. These findings align [7], who reported that precursor impurity levels strongly affect reaction selectivity and final API quality.

Industrial process optimization further improved precursor conversion performance through controlled reactant feeding systems and real-time temperature stabilization. Manufacturers implementing automated monitoring systems demonstrated lower variability in reaction efficiency compared to facilities relying on conventional batch-processing approaches. This trend reflects the growing adoption of Industry 4.0 principles within modern pharmaceutical manufacturing systems.

Relationship Between Reaction Kinetics and Industrial Sustainability

The findings of this study indicate that reaction kinetics optimization contributes not only to industrial productivity but also to environmental sustainability. Improved conversion efficiency directly reduces chemical waste generation, solvent usage, and energy consumption during API synthesis processes. Pharmaceutical manufacturing industries with optimized reaction systems produced lower waste volumes and demonstrated more efficient resource utilization.

The reduction of side-product formation also minimizes downstream purification requirements, thereby lowering operational energy demand and wastewater treatment burden. This aspect is particularly important because pharmaceutical synthesis frequently involves solvent-intensive purification stages that generate significant

environmental emissions [6], chemical industries remain major contributors to industrial carbon emissions due to high-temperature processing and extensive solvent utilization.

The integration of kinetic modeling and industrial trade data further provides a practical framework for sustainable industrial evaluation in developing countries. Since direct industrial process data are often confidential and difficult to access, publicly available trade statistics and industrial production datasets offer alternative indicators for assessing precursor utilization efficiency at the national scale.

The data-driven approach applied in this study also supports strategic policy development regarding pharmaceutical raw material management. By identifying precursor groups with lower conversion efficiency, policymakers and industries can prioritize research investment toward catalyst development, green solvent systems, and alternative synthesis pathways that improve industrial sustainability.

Furthermore, the increasing demand for domestic pharmaceutical production in Indonesia highlights the urgency of strengthening local precursor processing capability. Improving precursor conversion efficiency can reduce dependence on imported materials while simultaneously increasing national industrial competitiveness. Therefore, reaction kinetics analysis should be integrated more extensively into pharmaceutical manufacturing planning and industrial technology development programs.

4. Discussion

This study demonstrates that reaction kinetics parameters significantly influence the efficiency of pharmaceutical precursor conversion in active pharmaceutical ingredient synthesis processes. The findings confirm that precursor type, temperature conditions, catalyst concentration, solvent polarity, and precursor purity collectively determine industrial synthesis performance. These results are scientifically consistent with established chemical engineering principles and recent pharmaceutical manufacturing studies.

The superior conversion performance observed in ester-based precursor systems indicates that reaction pathway stability remains an important determinant of industrial synthesis efficiency. Esterification reactions generally involve predictable thermodynamic behavior and relatively lower activation energy barriers compared to more complex ketone or aromatic substitution reactions. As a result, industries utilizing ester intermediates can achieve more stable product yields and lower impurity formation.

Temperature optimization emerged as one of the most critical factors affecting precursor conversion. Increased temperature accelerated reaction rates by enhancing molecular kinetic energy and reactant collision frequency. However, the findings also indicate that excessive temperature conditions may promote precursor degradation and secondary side reactions. Therefore, pharmaceutical industries must balance temperature elevation with thermal stability considerations to maximize conversion efficiency without compromising product purity.

Catalyst utilization also demonstrated substantial benefits in improving industrial synthesis performance. Catalysts reduced activation energy requirements and accelerated selective product formation pathways, resulting in shorter reaction times and higher precursor utilization efficiency. This finding supports the increasing global adoption of catalytic pharmaceutical synthesis methods as part of green chemistry and sustainable manufacturing initiatives.

The role of precursor purity in determining conversion efficiency also deserves particular attention. High-purity precursor compounds minimized unwanted side reactions and facilitated more selective product formation. Conversely, impurities present within lower-quality precursor materials increased the probability of competing reactions and impurity generation, thereby reducing final API yield. This indicates that industrial precursor quality control remains an essential component of pharmaceutical manufacturing optimization.

From an industrial sustainability perspective, improving precursor conversion efficiency contributes directly to waste reduction and energy conservation. More efficient reactions require lower raw material input per unit of product generated, thereby reducing industrial resource consumption and environmental burden. Reduced solvent usage and purification requirements additionally support cleaner pharmaceutical manufacturing systems.

The integration of industrial trade statistics with reaction kinetics analysis represents one of the major contributions of this study. Most previous pharmaceutical synthesis studies relied primarily on laboratory-scale experiments without considering industrial precursor flow patterns. In contrast, this research demonstrates that publicly accessible industrial datasets can provide valuable information regarding precursor utilization trends and industrial conversion performance.

Nevertheless, several limitations should be acknowledged. The study relied primarily on secondary industrial and scientific datasets rather than direct industrial reactor measurements. Consequently, certain kinetic parameters were estimated using generalized industrial assumptions and literature-based modeling approaches. Future

research should incorporate direct industrial process monitoring, real-time sensor systems, and machine learning-assisted reaction prediction to improve analytical precision.

In addition, this study focused mainly on selected precursor categories under HS Code 29 commonly utilized in Indonesian pharmaceutical industries. Broader analysis involving additional precursor classes, industrial sectors, and comparative regional studies may provide more comprehensive understanding regarding pharmaceutical manufacturing optimization in Southeast Asia.

Overall, the findings suggest that reaction kinetics analysis can serve as an effective strategic tool for improving pharmaceutical manufacturing performance in developing countries. The integration of data-driven industrial evaluation, catalyst optimization, and sustainable synthesis principles may significantly enhance national pharmaceutical competitiveness while supporting environmentally responsible industrial development.

5. Conclusions

This study concludes that reaction kinetics characteristics play a critical role in determining the conversion efficiency of organic precursor compounds utilized in active pharmaceutical ingredient synthesis within Indonesian pharmaceutical industries. The analysis demonstrated that precursor type, operating temperature, catalyst concentration, solvent characteristics, and precursor purity significantly influence industrial synthesis performance and product yield stability.

Among the evaluated precursor groups, ester-based intermediates exhibited the highest conversion efficiency due to their stable reaction pathways and favorable thermodynamic properties. Temperature optimization between 60–90°C substantially improved reaction constants and precursor transformation rates while minimizing undesired side-product formation. Catalyst-assisted synthesis systems also enhanced precursor utilization efficiency by reducing activation energy requirements and increasing reaction selectivity.

The findings further revealed that high-purity precursor materials contributed significantly to higher API yield and lower impurity generation. Pharmaceutical manufacturers implementing controlled reaction systems and catalyst optimization strategies achieved better industrial efficiency compared to conventional synthesis approaches. In addition, improved precursor conversion efficiency supported industrial sustainability by reducing chemical waste generation, solvent consumption, and energy utilization.

This research also demonstrates that integrating industrial trade statistics, pharmaceutical manufacturing data, and reaction kinetics modeling provides an effective framework for evaluating industrial chemical performance in developing countries. The data-driven approach offers practical advantages because publicly available industrial datasets can be utilized to assess precursor utilization trends without requiring direct access to confidential industrial process information.

From a policy perspective, the study highlights the importance of strengthening domestic precursor processing capability and improving industrial synthesis efficiency to support pharmaceutical self-sufficiency in Indonesia. Optimizing precursor conversion may reduce dependence on imported raw materials while simultaneously improving industrial competitiveness and environmental sustainability.

Future studies are recommended to incorporate real-time industrial reactor monitoring systems, machine learning-assisted kinetic prediction, and broader precursor classifications to improve analytical precision and industrial applicability. Further investigation involving continuous flow synthesis systems and green solvent technologies may also contribute to the development of more sustainable pharmaceutical manufacturing processes in Indonesia and other developing countries.

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