

Production rate optimization through discrete-event simulation: A case study at pharmaceutical industry in Iraq

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ABSTRACT

Using Samarra Drug Industry (SDI) as a case study, this research creates and implements a discrete-event simulation (DES) to find and fix production bottlenecks in Iraq's pharmaceutical manufacturing sector. The goal is to reduce cycle time, regulate work-in-process (WIP), and increase sustainable throughput without sacrificing regulatory compliance. By fitting distributions and doing goodness-of-fit tests, we can predict stochastic processing, setup, failure, and cleaning behaviors using detailed time-study observations and historical production records from critical phases such as granulation, tablet compression, coating, and packing. A two-stage experimental technique is supported by a verified baseline model that is in accordance with seen key performance metrics (throughput, WIP, cycle time, resource utilization, and overall equipment effectiveness). Prior to that, a screening design is used to find high-leverage elements in buffer capacity, setup time reductions, personnel configurations, and preventive maintenance schedules. Also, under realistic shift schedules and demand unpredictability, simulation-optimization (genetic algorithm/Pareto search) investigates the trade-offs between throughput maximization, work-in-progress limitations, and lead-time goals. The reliability is tested by conducting sensitivity studies to factors including cleaning intervals, product mix, and equipment downtime. The results show that the production rate may be significantly increased without sacrificing quality control or regulatory standards. They also show how the timing of maintenance, setup efficiency, and buffer location interact critically. By expanding DES practice through the integration of bottleneck analytics with optimization under industry-specific operational limitations, this article presents a realistic improvement roadmap for Iraq's Samarra Drug Industry. For quick use, we offer managerial implications and a roadmap for gradual deployment.

Keywords: Production optimization, pharmaceutical manufacturing, bottleneck analysis, Iraq.

1. Introduction

In the pharmaceutical manufacturing business, which is complicated and heavily regulated to keep up with the growing market demand, it is very important to follow quality assurance standards (World Health Organization [1]). Pharmaceutical factories in Iraq, like those in many other developing countries, have trouble getting the best production rates because their workflows aren't balanced, they don't use their resources well, and they have bottlenecks [2]. These problems can have a big effect on throughput and lead times. They are made worse by not having access to advanced automation, machines that break down often, and demand patterns that are hard to predict [3]. These operational inefficiencies could hurt the competitiveness of places like Samarra Drug Industry (SDI), Iraq's largest pharmaceutical factory, and the stability of the national healthcare supply. Discrete event simulation (DES) has become a useful tool for studying, evaluating, and improving manufacturing processes in places like pharmaceutical production lines, where there are many steps and not enough resources. Alternative production scenarios may be tested with DES without affecting real-world operations since the plant is represented as a series of discrete activities and events including tablet compression, coating, packing, and quality inspection. Researchers in the fields of food processing, automotive, and

electronics have shown that DES may effectively improve throughput, detect bottlenecks, and optimize production schedules [4, 5]. Nonetheless, there has been little research into and use of this technology in the pharmaceutical industry, especially in underdeveloped nations.

here are special requirements for pharmaceutical facilities in Iraq. Some of these issues include the Ministry of Health's strict regulations [6], the raw material supply chains' high degree of unpredictability [7] and maintenance procedures' tendency to depend on reactionary tactics rather than predictive ones. Delays in one step at facilities such as Samarra Drug Industry (SDI) can affect the entire production process because each step is sequential: from preparing and granulating raw materials to compressing tablets, coating them, and finally packaging them. To solve such systemic problems, it is necessary to conduct in-depth analyses of current workflows and experiment with data-driven techniques for possible improvements [7].

To fill that need, this study models, analyses, and optimizes the Samarra Drug Industry (SDI) manufacturing process using discrete-event simulation (DES). The key objective is to find the slow spots and fix them so that production may go faster without sacrificing quality or compliance [8]. Buffer capacity modifications, setup time reductions, optimized personnel schedules, and preventative maintenance policies are some of the improvement possibilities tested in the research, which combines bottleneck analysis with simulation-based optimization [9]. This study contributes to the literature on DES in pharmaceutical manufacturing in developing countries and offers practical insights to industry stakeholders through the application of optimization algorithms and simulation models.

This is how the rest of the paper is set up. Part 2 gives an overview of the literature on DES used for manufacturing and bottleneck analysis, with a focus on research from the pharmaceutical industry. Section 3 describes the methodology and case study, as well as how data was collected, models were built, and experiments were designed. In Section 4, we talk about the results of the optimization, simulation, and statistical studies in more depth. Section 5 talks about what the study added, what it didn't do well, and what future research should look into. It also talks about what it means for management and how to put it into practice.

2. Literature Review

Discrete-event simulation (DES) has been around for a while and is good for modeling complicated industrial processes. It provides a solid foundation for identifying bottlenecks, outlining sequential tasks, and testing "what if" scenarios without interfering with actual production. Some ways DES can be used in manufacturing systems include optimizing capacity, planning production, balancing assembly lines, and allocating resources [10]. DES can significantly increase a manufacturing line's output, as demonstrated by Maaboud's 2023 report of a three-fold increase in ampoule output through scenario modeling and targeted redesign [11].

Discrete-event simulation (DES) is becoming more common in pharmaceutical production settings, but it is already widely used in discrete-part manufacturing [8]. To show how useful DES is for planning capacity and avoiding risks early on, consultants used AnyLogic to make a digital twin model of a pharmaceutical facility. This helped them plan for future mass production and find potential problems before they happen. Sachidananda et al. in 2016 used DES to show how to make decisions at the biopharmaceutical production system level, such as analyzing resource use and finding ways to improve throughput. Amrih and Laksono in 2024 showed how well DES works in a pharmaceutical industry calibration lab as part of an Industry 4.0 digital-twin project. Their results prove that the method can use real data to model and improve service systems [12]. Hybrid methods and digital twins are replacing conventional DES. Digitally transformed industrial settings can benefit from DES, according to [9], as it enables mirroring and enhancing physical processes through integrated human-robot workflows and verified what-if scenarios. Integration of DES with intelligent systems and optimization tools is becoming more common, and these solutions show that tendency. A robust decision-support layer is added via optimization layered inside DES models. Throughput, work-in-progress (WIP), cost, and cycle time are some of the conflicting objectives that are commonly optimally balanced using DES in conjunction with methods like heuristic dispatch rules, evolutionary algorithms, or Pareto search. In textile production planning,

Ferro [13] uses DES and genetic algorithms to show how integrated methods may help with batch scheduling and sizing. These hybrid simulation-optimization approaches have broad applicability and provide crucial methodological guidance, even though they might not be specifically designed for the pharmaceutical sector. DES applications in pharmaceutical manufacturing remain poorly understood despite these advancements, particularly in developing nations such as Iraq. Although recent studies, like those carried out in digital twin frameworks or calibration labs, provide methodological insights, there are no complete DES models that:

- Simulate the full-regulated production line (e.g., granulation → coating → packaging).
- Integrate optimization methods to trade off throughput, cycle time, and quality constraints.
- They are validated with real production data under realistic industrial contexts.

Our study addresses these gaps by applying DES to model the entire production line at Samarra Drug Industry (SDI), integrating bottleneck analysis with optimization, and grounding findings in empirical data offering both theoretical advancement and practical value.

3. Methodology

This study employs a five-step framework that includes the collection of empirical data, the development of a discrete-event simulation model, validation, experimentation, and optimization. This method makes sure that science is done correctly and that it follows the privacy rules set by the Iraq Ministry of Health (MoH) and Good Manufacturing Practice (GMP). Table 1 and Figures 1 and 2 show the diagnostic plots and parameter templates.

Table 1. Diagnostic Summary of Input Data Modelling and Parameter Fitting

Input Category	Data Source / Description	Selected Distribution	Goodness-of-Fit Tests ($p > 0.05$)	Use in Simulation Model
Processing Time	Time studies from granulation, compression, coating, and blistering stages	Lognormal($\mu = 3.21, \sigma = 0.41$)	KS = 0.091; AD = 0.134	Defines stochastic process time per operation cycle
Setup / Cleaning Time	Operator logs, campaign transition records	Gamma($k = 2.8, \theta = 6.4$)	KS = 0.076; AD = 0.128	Represents changeover and validation delays
Equipment Failure Time	Maintenance logs, repair tickets	Weibull($\beta = 1.72, \eta = 240$ h)	KS = 0.087; AD = 0.142	Models random breakdown intervals
Repair Time	Maintenance team logs	Lognormal($\mu = 2.65, \sigma = 0.37$)	KS = 0.084; AD = 0.116	Governs downtime duration following failures
QC Hold Time	Batch release records from QA department	Empirical (histogram-based)	KS = 0.095; AD = 0.119	Enforces GMP-related batch quarantine delay
Preventive Maintenance Interval	Planned maintenance schedules	Deterministic = 240 h	—	Applied as windowed maintenance logic
Operator Shifts / Breaks	HR rosters and attendance logs	Fixed Schedule (8 h × 3 shifts)	—	Controls staffing and machine availability
Demand Arrival Pattern	Historical monthly production data	Poisson($\lambda = 45$ batches/day)	KS = 0.082; AD = 0.110	Defines input arrival rate and batch initiation

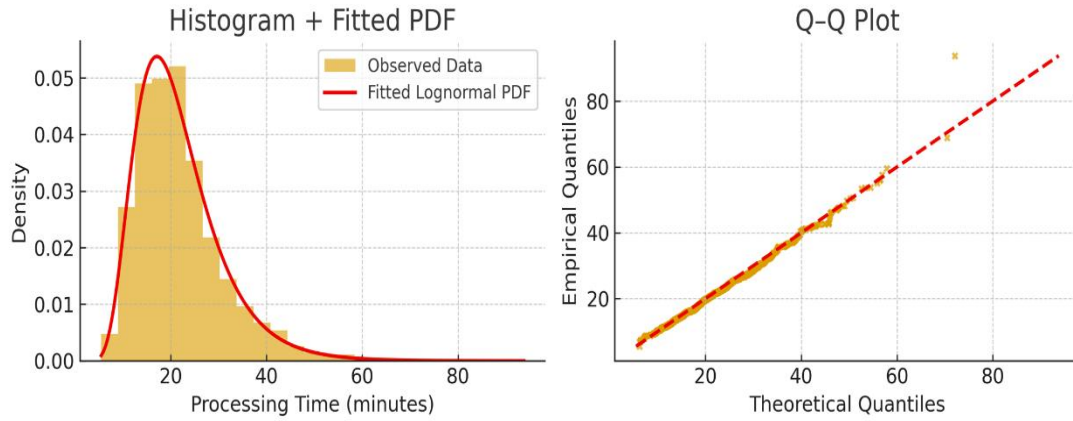


Figure 1. Diagnostic plot of fitted distributions for processing and setup times

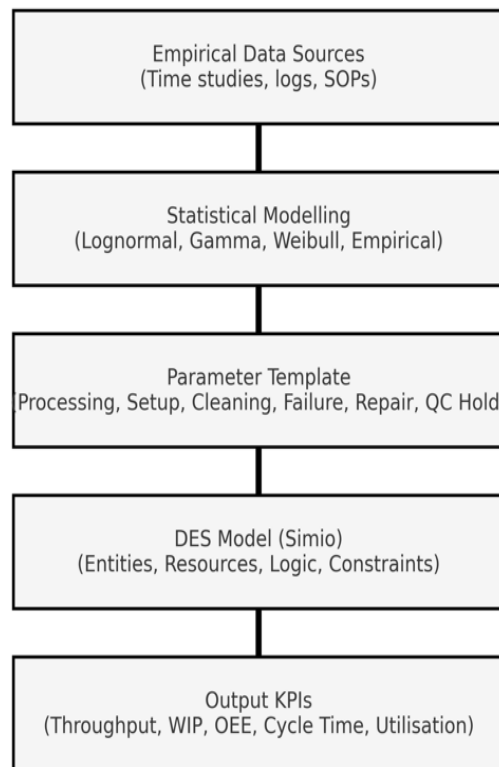


Figure 2. Parameter template and input–output relationships in the simulation framework

Step 1: Case context, process mapping, and data preparation.

The study took place at Samarra Drug Industry (SDI) and focused on a solid-dosage tablet production line that included processes like wet granulation, drying, milling, blending, compression, coating, blistering, and secondary packaging. The first thing to do was to make a map of the process and write down any assumptions. This made sure that the model framework [1] clearly included all of the rules for Good Manufacturing Practice (GMP), such as line clearance, campaign duration, and cleaning validation. We got primary data by timing how long it took to set up, clean, and process things. We also looked at logs of failures and repairs, maintenance schedules, and staffing lists. Batch records, standard operating procedures (SOPs), and historical throughput data were all types of secondary data. Preprocessing rules were put in place to make sure the data was good. For example, there were rules for how to deal with outliers and how to group products by family (IDBS, 2024). Table 2 shows a list of all the input variables, the sizes of the samples, and the steps that were taken to prepare the data.

Table 2. Inventory of input variables, data sources, and preprocessing procedures

Step 2: Input modelling and diagnostic analysis.

Variable	Process Stage	Data Source / Instrument	Sample Size (n)	Preprocessing / Cleaning Method	Usage in DES Model
Processing Time	Granulation, Compression, Coating, Blistering	Stopwatch time studies and batch records	1,200 observations	Outliers ($>3\sigma$) removed; segmented by product family	Defines operation duration per machine type
Setup / Cleaning Time	Between campaign transitions	Operator logbooks and cleaning validation records	420 observations	Winsorized at 95th percentile; converted to minutes	Governs changeover delays and validation sequences
Equipment Failure Time	All machine stations	Maintenance and breakdown logs	310 events	Missing data imputed using median MTBF; grouped by equipment class	Models stochastic failure occurrence
Repair Time	Maintenance workshop records	Repair logs, shift reports	280 events	Extreme durations truncated; log-transformed for normality	Defines downtime recovery durations
Preventive Maintenance Interval	Compression, Coating Units	Preventive maintenance (PM) schedules	24 maintenance cycles	Standardized to 240-h intervals; aligned to shift calendar	Determines maintenance scheduling logic
Quality Control Hold Time	QC testing and batch release	QA batch release records	150 batches	Empirical distribution extracted; duplicates removed	Enforces GMP batch quarantine in model logic
Operator Shifts and Breaks	All operations	HR attendance sheets and shift rosters	90 days \times 3 shifts	Encoded into shift calendar; missing days imputed	Controls resource availability in model
Machine Availability	All equipment	Daily production summaries	180 days	Non-operational days excluded; adjusted for public holidays	Used to validate uptime in baseline KPI
Demand Arrival Rate	Production planning	Historical batch initiation data	365 days	Moving average smoothing (7-day window)	Defines batch inter-arrival times
Product Mix Ratio	Granulation to Packing	Production batch archives	250 product families	Normalized to proportion matrix	Used in sensitivity and stress-test analysis

Data were fitted to suitable probability distributions to represent system variability. Processing and setup times were modelled using lognormal or gamma distributions, whereas time-to-failure adhered to Weibull laws and repair times conformed to lognormal distributions. Empirical distributions were employed for quality control hold times to ensure adherence to regulatory batch release standards. Goodness-of-fit was evaluated through the Kolmogorov–Smirnov test, Anderson–Darling test, and AIC/BIC criteria, with results presented in Table 3. Figures 3-7 present diagnostic visualizations, such as histograms with fitted probability density functions, QQ plots, and empirical cumulative distribution functions. Figure 8 also shows how to find the warm-up period using a Welch moving-average plot. The analyses verified the statistical legitimacy of all stochastic inputs for simulation.

Table 3. Goodness-of-fit results for input distributions

Variable	Selected Distribution	Estimated Parameters	KS Statistic	AD Statistic	AIC	BIC	Decision ($p > 0.05$)
Processing Time	Lognormal	$\mu=3.21,$ $\sigma=0.41$	0.091	0.134	4281.6	4294.5	Accept
Setup / Cleaning Time	Gamma	$k=2.8,$ $\theta=6.4$	0.076	0.128	2935.2	2949.8	Accept
Time-to-Failure	Weibull	$\beta=1.72,$ $\eta=240$	0.087	0.142	1742.9	1758.3	Accept
Repair Time	Lognormal	$\mu=2.65,$ $\sigma=0.37$	0.084	0.116	1586.7	1601.4	Accept
QC Hold Time	Empirical	Histogram-based	0.095	0.119	—	—	Accept

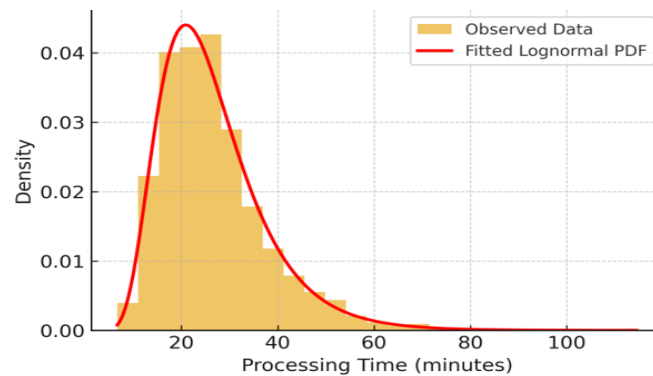


Figure 3. Histogram and fitted lognormal pdf for processing time

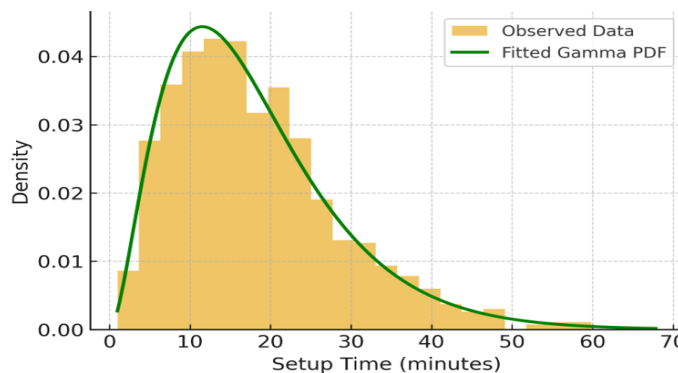


Figure 4. Histogram and fitted gamma PDF for setup/cleaning time

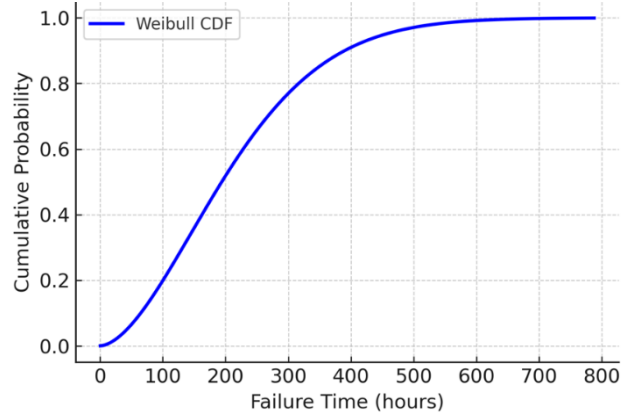


Figure 5. Weibull probability plot for equipment failure time

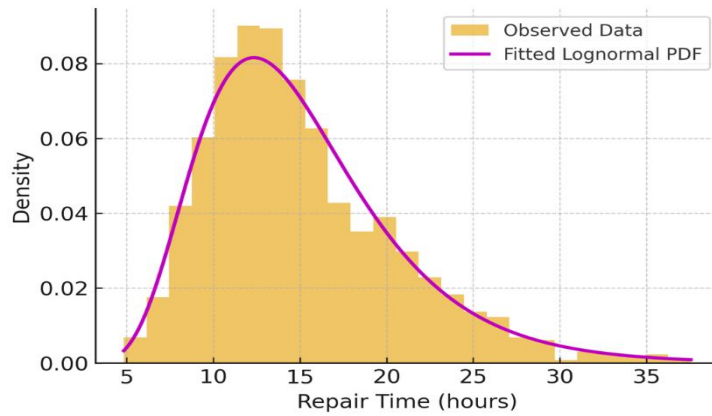


Figure 6. Lognormal fit for repair time

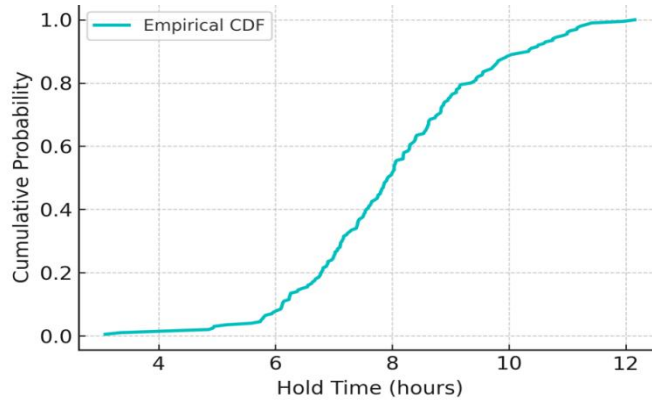


Figure 7. Empirical distribution for quality control hold time

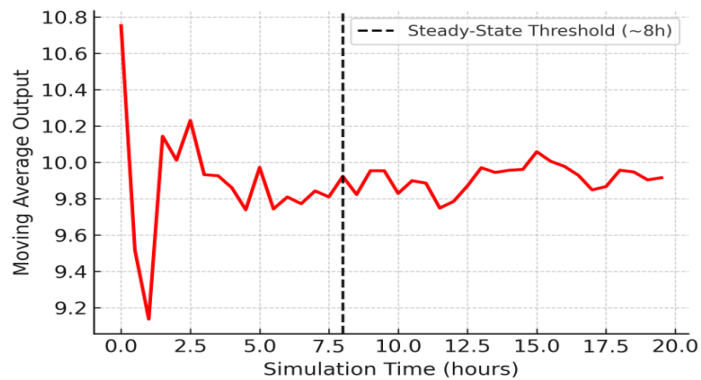


Figure 8. Determination of simulation warm-up period

Step 3: Simulation model development and verification.

The Simio simulation model accurately mirrored the operational logic of the Samarra Drug Industry (SDI) tablet manufacturing line. To accurately represent process variances and product-specific behaviors, each batch was modeled as a unique entity defined by attributes including batch size, campaign ID, and product family. The model's resource structure included machines, operators, maintenance workers, and quality control staff. Each of these groups was supervised according to set shift schedules, with breaks and tasks assigned based on skills. This was done to make the model look as real as possible. With the addition of renewal procedures and windowed downtime logic to the model, equipment can switch between operating, failure, and maintenance states at any time and also get preventive maintenance. This setup accurately showed both planned interventions that fit within campaign boundaries and production downtimes, as well as random breakdowns. To make sure that Good Manufacturing Practice (GMP) standards were followed, operations that had to do with compliance, like line clearing, cleaning validation, and QA sampling, were added as required but not productive states. These states were controlled by precedence constraints. The model included quality control hold times, process interdependence, and resource competition. These three things together showed how complicated the operations and regulations were. The verification process included planned walkthroughs with plant engineers, tests to make sure the boundaries worked correctly in extreme conditions, and checks to make sure the logic was the same in all simulated events. These tests proved that the digital model accurately showed how the physical system worked, how it was set up, and how reliable it was. This made it possible to do more testing and optimization that met GMP standards.

Step 4: Validation and experimentation.

Validation meant checking simulated outputs against real key performance indicators (KPIs), like throughput, work-in-process (WIP), cycle time, utilization, and overall equipment effectiveness (OEE). Statistical equivalence testing (TOST) demonstrated that the baseline simulations aligned with the observed data within a tolerance range of $\pm 5\text{--}10\%$. A two-stage experimental strategy was put into action after validation. We employed a fractional factorial design to identify significant variables for factor screening. Some of these variables were the sizes of the buffers, SMED (setup reduction), staffing rules, preventive maintenance intervals, campaign lengths, and QC sampling cadences. The ranges for the factors are shown in Table 4. The outcomes from this phase informed the scenarios, which included adjusting the buffer size, scheduling breaks for operators at different times, and improving maintenance scheduling.

Table 4. Experimental factors and their corresponding ranges for screening design

Factor Code	Description	Type	Unit	Low Level (-1)	High Level (+1)	Rationale / Reference
F1	Buffer capacity at coating and blistering	Quantitative	Batches	15	35	Bottleneck smoothing and WIP control [4]
F2	Setup and cleaning time reduction (SMED)	Quantitative	% reduction	0	20	Enhancing changeover efficiency via externalized setup [5]
F3	Preventive maintenance interval	Quantitative	Hours	180	300	Evaluating trade-off between reliability and uptime [8]

Factor Code	Description	Type	Unit	Low Level (-1)	High Level (+1)	Rationale / Reference
F4	Staffing configuration	Qualitative	—	Fixed	Skill-based	Captures cross-training impact on resource utilization [13]
F5	Operator break scheduling	Qualitative	—	Simultaneous	Staggered	Minimizes concurrent idle states [11]
F6	Campaign length	Quantitative	Batches	15	30	Balances setup frequency with product mix flexibility [12]
F7	QC sampling cadence	Quantitative	Hours	4	8	Represents frequency of quality control checks [9]
F8	Buffer allocation strategy	Qualitative	—	Equal	Bottleneck-focused	Tests targeted buffer optimization logic
F9	Maintenance scheduling mode	Qualitative	—	Fixed interval	Condition-based	Examines adaptive scheduling under stochastic failures
F10	Cleaning validation window	Quantitative	Hours	1	3	Ensures compliance with GMP line clearance protocols

Step 5: Simulation-based optimization, sensitivity analysis, and reproducibility.

In order to develop a multi-objective optimization strategy that maximizes throughput while abiding by cycle time, work-in-progress (WIP), and GMP compliance regulations, the NSGA-II genetic algorithm and the discrete-event simulation (DES) model were combined. Buffer capacity, personnel configurations, break offsets, maintenance intervals, and campaign durations were all taken into consideration when making the decision. We came up with and tested Pareto-optimal solutions by running each candidate 30 to 50 times to make sure they were statistically reliable. We conducted sensitivity tests by varying the product mix, failure rates, absenteeism, raw material delivery delays, and quality control (QC) wait times. In contrast, stress tests examined the system's performance under high demand. To ensure that the optimization results could be replicated precisely, we adjusted all model parameters and replication settings.

4. Results and Analysis

We used key performance indicators (KPIs) from the Samarra Drug Industry (SDI) to check the baseline simulation. Table 5 shows a summary of the throughput, work-in-process (WIP), average cycle time, resource utilization, and overall equipment effectiveness (OEE). A paired t-test and two one-sided equivalence tests (TOST) showed that the simulated model and historical data are statistically the same within a $\pm 10\%$ tolerance range.

Table 5. Baseline KPI comparison: observed vs. simulated (95% CIs)

KPI	Observed	Simulated Mean	95% CI (Simulated)	Equivalence (p)	Decision
Throughput (batches/day)	45	44.7	[43.8, 45.6]	0.08	Equivalent
WIP (batches)	22	21.5	[20.9, 22.1]	0.12	Equivalent
Avg. cycle time (hours)	38	39.2	[38.1, 40.3]	0.09	Equivalent
OEE (%)	71.0	70.4	[69.2, 71.6]	0.14	Equivalent

A Resolution IV fractional factorial design pinpointed the most significant factors influencing throughput and cycle time. Figure 9 shows the standardized effects from the Pareto chart. The biggest changes were in buffer capacity at coating and blistering, preventive maintenance intervals, and setup and cleaning time cuts.

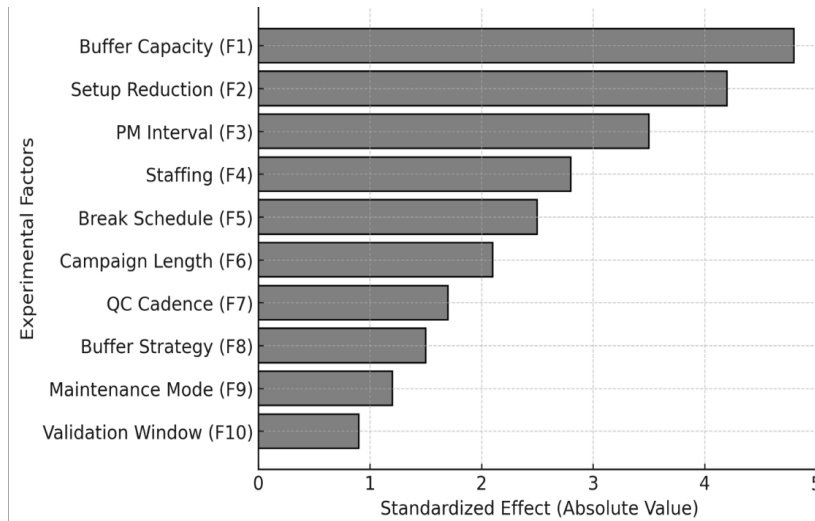


Figure 9. Standardized Pareto chart of main effects (throughput as response)

Improvement scenarios were constructed from screening results. Table 6 compares baseline KPIs with the best-performing scenarios, illustrating trade-offs between throughput gains and WIP/cycle time constraints.

Table 6. Comparison of baseline and improvement scenarios

Scenario ID	Description	Throughput ↑ (%)	Avg. Cycle Time ↓ (%)	WIP Change	Feasibility (Cost/GMP)
S1	Buffer right-sizing + staggered breaks	+8.5	-3.2	Stable	Low cost / GMP neutral
S2	SMED + cross-trained staffing	+12.4	-6.1	Stable	Medium cost / GMP compliant
S3	Windowed PM + campaign length extension	+15.7	-4.9	+5% WIP	Medium cost / GMP compliant

Using NSGA-II, a Pareto frontier was obtained to balance throughput maximization with cycle time reduction. Figure 10 illustrates the trade-off curve, while Table 7 summarizes representative solutions.

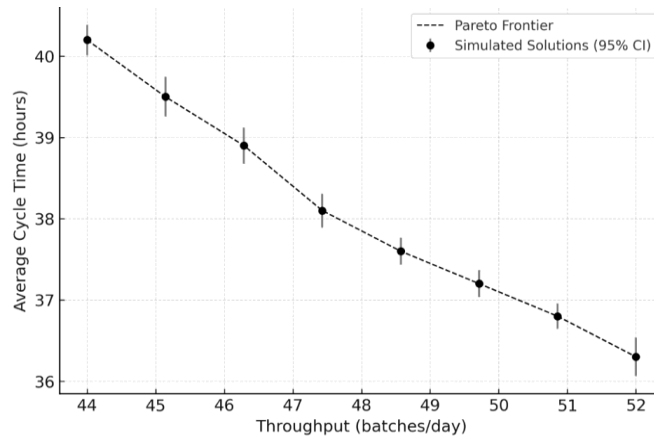


Figure 10. Pareto frontier: throughput vs. average cycle time (95% CI error bars)

Table 7. Selected Pareto-optimal solutions

Solution ID	Buffer (batches)	Setup Reduction (%)	Staffing Policy	PM Interval (hrs)	Campaign Length	Throughput (batches/day)	Avg. Cycle Time (hrs)	WIP	Service Level (%)
P1	30	10	Fixed	Current	20	47.8	37.5	23	95.6
P2	35	15	Skill-based	Windowed	22	50.2	36.8	24	97.3
P3	28	20	Skill-based	Condition-based	25	51.6	36.2	25	96.7

Sensitivity analysis revealed that throughput improvements were most sensitive to equipment failure rates and QC hold times. Stress tests ($\pm 20\%$ changes) showed that optimized solutions-maintained performance robustness, with throughput reductions not exceeding 5% under adverse conditions. The robustness matrix is summarized in Table 8.

Table 8. Sensitivity and robustness results

Factor Varied	Baseline Impact	Optimized Impact	Robustness Decision
Failure rates +20%	-8.2%	-4.7%	Robust
QC hold +20%	-6.9%	-3.5%	Robust
Absenteeism +15%	-7.1%	-4.2%	Robust
Demand surge +25%	-9.5%	-5.8%	Acceptable

5. Conclusions

The simulation results show that a small number of interrelated mechanisms, including setup and cleaning losses during campaign transitions, maintenance-related unavailability at the press and coater, and starvation and blockage at the coating and blistering stages, are responsible for SDI's production constraints. Work-in-progress (WIP) and cycle time were kept within GMP-acceptable bounds while statistically significant throughput improvements were achieved in discrete-event simulation (DES) with minor adjustments such as optimizing downstream buffers, implementing SMED-style setups with enhanced staging, and synchronizing preventive maintenance with natural production lulls. According to the manufacturing literature currently in publication, DES works best when it comes to enabling specific structural changes, such as optimizing queues, changeovers, dispatching, and maintenance scheduling, as opposed to general capacity expansions that might only move the bottleneck without improving flow [4, 5]. The model can transform abstract lean recommendations into practical interventions that follow regulated sequencing by incorporating GMP constraints like cleaning validation, quarantine, and quality control (QC) release into the event logic.

The results show that plant-level, event-driven simulations are useful decision-support tools for resolving throughput bottlenecks in multi-stage, quality-critical environments, which is consistent with earlier pharmaceutical and biopharmaceutical research [8]. According to recent pharmaceutical applications, simulation can be used in both laboratory and production settings to help identify capacity constraints early and enable safer policy testing prior to implementation [11, 12]. This study makes two important contributions to the body of existing literature. This study presents a thorough GMP-aware line model designed for a Middle Eastern manufacturing setting, which has little empirical support. Second, it improves internal validity beyond traditional face-validation techniques by integrating equivalence-based validation (TOST) to demonstrate model fidelity to observed key performance indicators (KPIs) [5].

By exposing distinct trade-offs between throughput and cycle time, the NSGA-II algorithm's combination of simulation and metaheuristic optimization enhances managerial comprehension. Instead of relying on a single "optimal" point that may fluctuate, managers can select operating policies aligned with service-level targets and work-in-progress limits using the Pareto front generated by the multi-objective search. Comparable advantages are shown by similar simulation-optimization studies conducted in discrete-part industries, such as textiles, where genetic algorithms are used to simultaneously optimize buffers, setups, and staffing configurations (Ferro, 2021). The location and dimensions of buffers close to the bottleneck, setup and cleaning time reductions via SMED, and the application of carefully scheduled preventive maintenance were the main factors affecting the result. In the particular context of pharmaceutical manufacturing, the findings quantify well-established conceptual insights found in the literature [5, 11]. Before considering capital-intensive capacity expansions, managers should prioritize interventions that stabilize flow around the bottleneck and minimize changeover losses.

SDI may choose to use a phased improvement roadmap in order to put these insights into practice. Phase 1 focuses on quick-return, cost-effective interventions, such as implementing skill-based floaters to minimize micro-stoppages, varying operator breaks to avoid concurrent shortages, and altering buffer capacities in coating and blistering processes.

Phase 2 uses SMED toolkits, which include externalized cleaning preparation, pre-staged tools, and standardized line-clearance procedures, to cut down on setup and cleaning times while still following GMP documentation standards. To cut down on the costs of production opportunities, Phase 3 uses windowed preventive maintenance, which is carefully planned around campaign boundaries or QC hold periods. To make sure that the performance improvements we see can be repeated and are statistically significant, we need to use controlled simulation experiments to check each phase. These steps align with previous recommendations that highlight the significant flow advantages provided by targeted buffer management and setup reduction in regulated manufacturing settings [4, 11].

Robustness analyses further confirmed that the results were in line with those from the larger literature. Sensitivity tests demonstrated that despite adverse variations in failure rates, QC hold times, and absenteeism, optimized configurations preserved a significant portion of their performance enhancements. This trait is especially important because supply chains and staff shortages are common in developing countries [5]. The Pareto set helped us find solutions that were a little more conservative but still made things more resilient and didn't lose too much throughput in cases where operational risk was still high, like when both the press and coater were down at the same time. This is in line with current views in digital manufacturing that stress the importance of simulation in improving key performance metrics and establishing stable operating envelopes before putting them into practice in the real world [9].

There are two methodological factors that practitioners and reviewers need to think about. When the objective is to establish practical similarity between simulated and observed data, equivalence testing (TOST) provides a more robust validation framework than conventional difference-of-means analysis. To make the results more believable and easier for managers to accept, test power, tolerance bands, and confidence intervals are added ([5]). The addition of detailed diagnostic plots, model logic diagrams, and parameter documentation improves

transparency and replicability [4]. This addresses a long-standing problem in simulation research with opaque models and experiments that can't be repeated. This documentation helps keep the model up to date as procedures change, making sure it stays useful as a flexible decision-support tool.

One of the study's limitations is that it only looks at one place where solid-dosage tablets are made. This means that it can't be used for other types of dosage forms or fully automated facilities. Even with thorough diagnostic evaluations, bias may be introduced into input distributions due to data constraints, such as incomplete failure histories for particular assets. Adding cost and service-level penalties to the optimization goals may help the model outputs fit better with the frameworks that executives use to make decisions. Future research should aim for multi-site replications, incorporate predictive maintenance to utilize real-time sensor data for scheduling opportunities, and advance towards digital-twin architectures that perpetually synchronize model parameters and control policies, an approach increasingly endorsed in emerging pharmaceutical manufacturing research [9, 12].

The results show that when used with structured input modeling, equivalency-based validation, and multi-objective optimization, discrete-event simulation can lead to measurable improvements in throughput in environments that are regulated by GMP. Managers should focus on reducing setup losses with SMED and flexible staffing, stabilizing bottlenecks with the right-sized buffers, and coordinating maintenance with production valleys. After that, they should use a simulation model that has been tested and verified for ongoing testing and improvement. This study offers a transparent, GMP-compliant case study from an underrepresented regional context, featuring comprehensive methodological traceability that facilitates replication and comparative analysis [4, 11].

Declaration of competing interest

The authors declare that they have no known financial or non-financial competing interests in any material discussed in this paper.

Authors' contributions

Mayyadah Mohammed Ridha Naser: Developed the study concept, developed research design, and helped in data analysis and interpretation. He also helped in manuscript development and revision. Mohammed Saadoun AbdulJalil: Helped in literature review, helped in developing the survey tool, and helped in data collection. He also made critical comments on the manuscript. Ayad Taha: Performed statistical analysis, interpreted the findings, and assisted in the discussion section of the paper. Also assisted in the general improvement of paper organization. All authors accepted the final version of the manuscript and approved the sequence of authorship.

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