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Gray Relational Analysis of Tuberculosis Drug Interactions A Multi-Parameter Evaluation of Treatment Efficacy

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Abstract

This study employs Gray Relational Analysis (GRA) to develop an optimized mutation list for drug susceptibility testing (DST) in tuberculosis. While phenotypic DST remains the reference standard, it requires sophisticated laboratory infrastructure and takes over a month, making it impractical in many settings. As an alternative, we analysed whole-genome sequencing data from a globally diverse set of isolates to create a genotypic resistance prediction framework aligned with WHO guidelines. Our methodology improves upon previous approaches by incorporating new and repurposed drugs excluded from earlier reviews and addressing limitations of arbitrary genomic region selection in Sanger sequencing. The analysis targets Genes that encode proteins associated with drug metabolism, receptors, transport mechanisms, and oxidative stress response, which significantly impact drug responses and disease susceptibility. We evaluated process parameters including completeness, accuracy, efficacy, and applicability. The GRA method effectively transforms multiple objectives into a single performance measure, enabling optimal parameter selection while addressing complex interactions between multiple factors. This research contributes to achieving whose global TB targets by providing a standardized mutation list that enables rapid, accurate diagnosis, allowing patients to promptly begin the most effective treatment while overcoming the limitations of time-consuming phenotypic testing.

Keywords: Tuberculosis, Drug Susceptibility Testing, Whole-Genome Sequencing, Mutation List, Genotypic Resistance, Multi-attribute Decision-making, Mycobacterium tuberculosis complex, Antimicrobial Resistance, WHO Guidelines

Introduction

WHO has set a significant but the challenge is to target universal drug susceptibility testing (DST), which includes both new and repurposed drugs under the revised definition of extensively drug-resistant tuberculosis. While phenotypic DST is Reference standard for most drugs, it is time-consuming, often taking More than a month, requiring expensive, state-of-the-art laboratory infrastructure constraints that make it impractical for many countries. In contrast, genetic susceptibility testing offers a fast, an accurate, automated and cost-effective alternative. However, there is currently no WHO-approved list of mutations interpreting genomic DST results. Alignment with WHO policies supporting rapid, accurate diagnostic tools is expected to have a significant global impact. Previously, WHO published guidelines for interpreting MTBC next-generation sequencing data, recognizing the results of an earlier systematic literature review? However, that review excluded new and repurposed drugs and was based on Sanger sequencing, where the selection of genomic regions was arbitrary, increasing the risk of false positives. As a result, knowledge gaps exist. To address these gaps and establish a mutation list for the first WHO-approved anti-TB drugs, we conducted a systematic analysis of a large, globally diverse set of isolates, using whole-genome sequencing (WGS) data with DST [1]. To achieve the five-year global TB targets, optimal Use of existing and new diagnostic and therapeutic tools essential. To ensure timely and accurate diagnosis and to enable patients to start the most effective treatment promptly, The WHO tuberculosis strategy emphasizes universal access to drug susceptibility testing. However, phenotypic testing for M. tuberculosis is time-consuming, often taking more than a month, and requires an expensive, sophisticated laboratory infrastructure with strict bio security measures.

Over the past two decades, highly specific and sensitive genotyping methods, Nucleic acid amplification tests and whole-genome sequencing etc., have significantly transformed the diagnosis of tuberculosis. To establish a global standard for genotypic resistance prediction, WHO launched the first version of the mutation list in 2021? The list was developed based on the analysis of 41,137 Mycobacterium tuberculosis complex isolates from 45 countries, which included both drug susceptibility testing and WGS data. The misuse of antibiotics in China has led to diverse and complex drug resistance patterns. For example, quinolone antibiotics are widely used to treat respiratory, gastrointestinal and urinary tract infections over the past few decades. As a result, the high resistance rate of quinolones in China is primarily due to their easy availability and misuse for non-tuberculosis infections comprehensively characterize drug-resistant mutations in China, we developed a list of Mycobacterium tuberculosis complex drug-resistant mutations using methods linked to the first edition of the 2021

WHO list [2]. Errors in medication administration are common occurrences in hospitals and remain a significant concern serious problem, occurring in Between 3% and 7% of doses administered by nurse's result in approximately 4,000 preventable injuries per hospital each year. As a result, these errors are less likely to be detected and more likely to directly affect patients compared to other forms of medication errors. Drug infusions pose a particularly high risk due to complex dose calculations, including rate and timing, as well as the necessity of managing multiple infusions simultaneously the same time. Many high-risk drugs, such as Insulin infusions, narcotic infusions, vasopressors, and electrolytes like potassium in parenteral nutrition, are commonly administered by infusion. It found that 20% of critically ill adults experienced healthcare-related injuries, half of these incidents were preventable, and 61% resulted in injuries attributable to medication use [3]. Ensuring the availability and replenishment of medicines in District Health Department pharmacies, Puskesmas, Sub-Puskesmas and other health service units such as Bos Yandu or First Level Health Facilities (FKTP) is essential for maintaining and improving health quality. Therefore, ensuring access to safe, effective, high Accessible, cost-effective medicines in appropriate forms and adequate doses is very important. Managing pharmaceutical supplies, including medicines, to meet service requirements involves a series of processes such as planning, purchasing, requisitioning, Handling, storing, distributing, regulating, documenting, reporting, archiving, monitoring, and assessing [4]. COSMIC, or Catalo the Somatic Mutations in Cancer Database collects information on the effects of somatic mutations in various human cancers.

As previously mentioned, its primary data is manually curated by experts who review the scientific literature, extract detailed mutation information, and include additional relevant factors such as environmental influences and patient prognosis. Along with extensive manual duration, the second pathway integrates large-scale but highly targeted data into COSMIC, derived from major cancer data portals and downloadable files linked to supporting tables and selected studies. The combination of these two data pathways provides COSMIC with unparalleled breadth and depth, establishing it as a leading resource for exploring the ethology and mutational landscape of human cancers. Genetic predispositions Common diseases and differences in drug response are primarily affected by frequent genetic variations, with single nucleotide polymorphisms being the most prevalent (SNPs), are estimated to occur every few hundred bases throughout the human genome. Extensive genome-wide screening programs have identified nearly a million SNPs, which are now listed in databases. However, instead of conducting genome-wide analyses, we focused on specific regions containing genes of interest, particularly proteins involved in drug metabolism, drug receptors, transporters, and molecules that respond to oxidative stress. These genes are significantly impact on drug response, you will also be susceptible to common diseases like atherosclerosis and diabetes [5, 6]. Large-scale genome-wide screening programs have catalogued nearly a million SNPs in databases. However, instead of conducting comprehensive genome-wide analyses, we focused on specific regions containing genes of interest, particularly those involved in drug metabolism, drug receptors, transporters, and oxidative stress response. These Genes likely play a key role drug response, it can also affect susceptibility to common diseases such as atherosclerosis and diabetes.Extensive genome-wide screening programs have listed nearly a million SNPs in databases. However, instead of conducting genome-wide analyses, we targeted specific regions containing genes of interest, particularly those involved in drug metabolism, drug receptors, transporters, and oxidative stress response.

These genes are expected to play important roles in drug response, you will also be susceptible to common diseases like atherosclerosis and diabetes [7]. Single-nucleotide polymorphisms are important markers for detecting genes linked to common diseases and advancing personalized medicine. In the future, comprehensive genome-wide SNP maps will help researchers analyse DNA variations and Forecast an individual's reaction to a particular medication treatments. This effort led to the generation of integrated genomic maps for 145 target regions including SNPs and other genetic variants. Plasma membrane-bound molecules that trigger cellular responses to various extracellular signals are promising Targets for therapeutic medications. The G-protein-coupled receptor (GPCR) family is among the most extensively researched drug receptor groups. Regulating GPCR activity has contributed to the successful creation of a wide range of therapeutic medications that are already commercially available. In fact, recent estimates suggest that GPCRs serve as targets for approximately 50% of all modern drugs [8]. We aimed to improve the 2015 Microbial Prediction Index in several ways. First, we sought to create a clean code. Second, we wanted to allow users to define their own anti-lists.

Latest version of the Microbial Prediction Index, which has been continuously updated since its release, derived from research by Walker et al., who examined same 3,500 samples used in the original performance evaluation. However, No independent testing or validation dataset is available to accurately estimate error rates. Finally, we aim to improve support for I War data by refining the statistical model, although the test was limited to five replicates of a single M. bovid BCG strain. The species-identification method remains unchanged; however, following its release, Microbe Predictor underwent extensive evaluation by Public Health England (PHE), which led to improvements to meet their acceptance criteria in species-informed studies. While we report on the prospective use of these methods at PHE, this review focuses primarily on improvements in resistance prediction. Initially, we combined the resistance list from The Cryptic Consortium et al. with the existing second-line drug resistance list from Walker et al. This combined list serves as our initial candidate, which is being continuously refined and evaluated on successive datasets [9]. From another perspective, bacteria beyond E. coli have been attracting attention as cell factories due to their metabolic diversity and biosynthesis capabilities,

which have evolved through adaptation to diverse environments. Features such as Improved solubility in halophile and lime-dependent bacteria, improved secretion in lactic acid bacteria, Endotoxin-free Gram-positive species and post-translational modifications in mycobacteria make them very promising for protein production, especially for challenging-to-express proteins. Although these alternative bacterial species share some limitations with prokaryotic-based production, their study should not be overlooked. Instead, they should be actively supported, as they not only broaden the range of available cell factories but also offer new opportunities for scalable and easily cultured systems that may present fewer methodological challenges than conventional protein production platforms [10]. METLIN offers robust search capabilities, allowing users to easily access relevant data from it'sa comprehensive collection of metabolic data and MS information. The query process is straightforward and user-friendly, allowing users to access all LC/MS data related to a specific cancer type with a single click. For advanced searches, multiple parameters can be specified, including m/z and retention time intervals, ionization mode, sample characteristics, or bio fluid type. Scientists can also explore individual samples Stored in a database, it displays information such as age, gender, disease stage, bio fluid or tissue type, and ionization method, and peak count. The second challenge involves managing the large volume of collected metabolic mass spectrometry data bio fluid analysis, which is an area of active research for commercial and academic groups [11]. In recent years, porphyries and related compounds have received significant attention as therapeutic agents.

They play an important role in medicine, especially in cancer detection and as photosensitizers for photodynamic cancer therapy. In addition, their potential applications have expanded to the treatment of various malignant conditions, including psoriasis, arterial blockages, and viral and bacterial infections such as HIV. The biological effects of porphyries are primarily influenced by their physicochemical properties, which significantly affect their photo physical behaviour. In particular, aggregation and axial binding alter their absorption characteristics, quantum efficiency, and luminescence duration, and triplet state lifetime. When injected into the bloodstream as concentrated solutions, porphyries may experience reduced activity or may cause adverse effects. In addition, interactions with large molecules may limit their efficacy and bio distribution, as they are mainly localized in the cytoplasm and exhibit weak binding to cell membranes [12]. Unlike single gene disorders such as Huntington's disease, complex diseases typically arise from There is a combination of genetic and environmental factors, each contributing to increased susceptibility to this condition? Purpose GWAS Aims to detect SNPs in linkage disequilibrium with genes or regulatory elements that may harbour causal variants that contribute to the etiological factors of a condition, even in the absence of a definitive causal variant. Unlike candidate gene studies, GWAS uses a whole-genome approach, analysing large populations, sometimes numbering in the hundreds of thousands, to examine traits such as disease susceptibility, drug response, and anthropometric features [13].

Considerable evidence suggests that changes in cancer-related genes can greatly affect clinical outcomes in anti-cancer treatments. For example, targeting protein production from the BCR–ABL translocation in chronic myeloid leukaemia or targeting the BRAF gene in malignant melanoma has revolutionized treatment approaches and significantly improved survival rates. In addition, even among carefully selected patients, clinical responses vary widely and are not fully understood. This highlights the need to develop Enhanced biomarkers to more effectively guide treatment decisions and enhance clinical outcomes [14]. The primary goal of investing in health research is to advance scientific knowledge and improve health outcomes. However, to effectively translate research findings into practical benefits and further research, reliable and accessible data are essential. Peer-reviewed research articles play a key role in validating scientific findings and disseminating them to the research community and clinical practice. Without publication, research often goes unnoticed. However, too often, these articles fail to clearly communicate how the research was conducted, what was discovered, the reliability of the findings, and their relevance in the broader scientific context. As a result, many published studies do not effectively fulfil their intended purpose.

Over the past 15 years, various reporting guidelines have been developed to ensure clarity and completeness in research studies. These guidelines outline the essential information needed to accurately describe the methodology and findings of a study, particularly highlighting factors that may introduce bias. Most internationally recognized guidelines are based on expert consensus, involve methodologists and journal editors, and are supported by relevant empirical evidence. They serve as a complement to scientific writing recommendations for authors and journal guidelines [15].

Materials and Method

Rifampicin: Rifampicin a broad-spectrum antibiotic used to treat tuberculosis (TB) and other bacterial infections by blocking bacterial RNA synthesis, thereby preventing bacterial replication. Often combined with other antibiotics, it helps reduce the risk of drug resistance. In addition, rifampicin is used to treat leprosy, meningococcal infections, and some staphylococcal infections. Common side effects include liver toxicity, gastrointestinal problems, and red-orange discoloration of body fluids. By inducing liver enzymes, rifampicin alters the metabolism of many drugs. Due to its potency and resistance concerns, its use is strictly monitored, and it is essential to follow the prescribed regimen.

Isoniazid: Isoniazid is a primary antibiotic for the treatment and prevention of tuberculosis (TB). It works by inhibiting the production of my colic acid, a key Component of the bacterial cell wall, leading to destruction Mycobacterium tuberculosis. It is usually used in combination with other tuberculosis drugs, which helps reduce the risk of drug resistance. Common

adverse effects include liver toxicity, peripheral neuropathy, and digestive problems. To reduce the risk of neuropathy, vitamin B6 (pyridoxine) is often co-administered. Metabolized in the liver, its effectiveness depends on genetic variants that affect enzyme activity. Strict adherence to the prescribed regimen is essential to ensure successful treatment outcomes.

Levofloxacin: Active against both Gram-positive and commonly prescribed for Gram-negative bacterial infections pneumonia, sinusitis, and complicated It is used to treat urinary tract infections with nausea, diarrhea, headache, and common side effects. an increased risk of muscle atrophy. It may also May lead to central nervous system effects, including dizziness or confusion. Due to concerns about resistance and side effects, its use is closely controlled in clinical practice.

Moxifloxacin; Moxifloxacin a broad-spectrum fluoroquinolone antibiotic prescribed for treating various bacterial infections, including respiratory, skin, and intra-abdominal Infections caused by inhibition of bacterial DNA gyrase and topoisomerase IV, disruption of DNA replication and bacterial proliferation. Active against both Effective against both Gram-positive and Gram-negative bacteria, moxifloxacin is commonly prescribed for pneumonia, bronchitis, and severe Skin infections, with common side effects including nausea, diarrhea, headaches, and a risk of tendonitis or tendon rupture. It may also May result in central nervous system side effects like dizziness or confusion. Due to concerns about resistance and potential side effects, its clinical use is closely regulated.

Etambutal: Ethambutol is an anti-tuberculosis antibiotic used to combat Mycobacterium tuberculosis infections. It works by inhibiting arabinose transferees, an enzyme important for bacterial cell wall synthesis, thereby inhibiting bacterial growth. It is usually prescribed with other tuberculosis drugs to help prevent drug resistance. A significant adverse effect is optic neuritis, which can lead to visual disturbances such as blurred vision and colour blindness. Additional side effects include joint pain, gastrointestinal problems, and liver toxicity. Regular eye examinations are advised during treatment. Given its importance in the treatment of tuberculosis, strict adherence to the prescribed regimen is essential to achieve successful treatment results.

Completeness: Completeness refers to the state of completeness, ensuring that all essential elements are present and nothing is missing. It indicates that every element necessary for a specific purpose or to meet a need has been included. In mathematics and logic, completeness refers to ensuring that all valid statements within a system can be derived using its principles. In various fields, such as data analysis, it refers to the presence of all relevant information. In personal and professional settings, achieving completeness in tasks, projects, or relationships improves performance and satisfaction. Striving for perfection promotes accuracy, reliability, and overall success in various aspects of life.

Accuracy: Accuracy refers to the degree of correctness, precision, and reliability in data, measurements, or actions. It ensures that results closely match the true or intended value, minimizing errors and discrepancies. In science and engineering, accuracy is fundamental to reliable data and informed decision-making. In communication and reporting, it strengthens credibility and trust. Accuracy is equally important in everyday activities such as financial calculations and medical diagnoses, where even small errors can have significant impacts. The pursuit of accuracy improves efficiency, consistency, and overall performance. It is often combined with precision, which emphasizes consistency and repeatability in measurements or processes.

Efficacy: Efficacy refers to the ability of a procedure, treatment, or intervention to achieve a desired outcome under ideal or controlled conditions. It is widely used in the medical and pharmaceutical fields to assess how effectively a drug or treatment delivers its intended results. More broadly, efficacy applies to strategies, technologies, and policies, determining their success in achieving established objectives. High efficacy indicates strong performance and reliability, while low efficacy indicates areas for improvement. This is distinct from efficiency, which considers real-world variables. Improving efficacy in any domain improves outcomes, improves efficiency, and increases overall success by refining processes and reducing failures.

Applicability: Applicability refers to the suitability and appropriateness of a concept, rule, or method within a specific context or situation. It assesses whether a policy or solution can be effectively implemented to achieve a specific outcome. In fields such as law, science, and technology, applicability ensures that theories, techniques, or regulations are practical and advantageous. A high level of applicability indicates broad applicability, whereas limited applicability indicates limitations in certain conditions. Assessing applicability supports decision-making by aligning approaches with real-world needs. It is essential in problem-solving, innovation, and policymaking, improving efficiency and effectiveness in various fields.

GRA Method

The gray relation analysis (GRA) method initially introduced by Deng was designed to address the multi-attribute decision-making challenge by choosing the alternative with the highest gray relation degree for the highest for the positive ideal solution and the lowest for the negative ideal solution. Kung and Wen applied GRA to examine the gray MADM issue in venture capital firms, while Guo, Yang, and Huang used it for facility organization and dispatch rule selection. Chiang extended GRA to calculate dependency criteria in MADM problems. In addition, Malek, Ebrahimnejad, and Tavakoli-Moghaddam proposed an improved hybrid GRA method for green redistribution. Alptech and Sarak evaluated low-carbon development in various countries using the GRA model. Yazdani, Kahraman, Zarate, and Onar improved the decision-making process by integrating integrated quality function deployment with GRA to determine critical supply chain drivers in a fuzzy system. Tan, Chen, and Wu. used GRA with AHP to analyse green design alternatives. Meanwhile, Liang,

Darko, and Xu devised a PFMCGDM-based approach to evaluate commercial bank credit risk using GRA [16]. The Taguchi method optimizes parameters based on the signal-to-noise ratio, where a higher ratio indicates a closer approximation to the optimal state.

However, it is limited to optimizing a single response and becomes ineffective when multiple responses need to be considered. In many situations, the Parameters cannot be defined for a single response, as some responses need to be minimized while others need to be maximized. As a result, multiple response optimization is necessary for the current research. The Gray Relational Analysis approach is applied to address this requirement.This method effectively addresses the complex interactions between multiple performance attributes. Multiple response optimization transforms combine multiple objectives into a single objective. Through GRA, a gray relational grade is calculated to assess various performance attributes, simplifying complex attributes into a single performance measure. The GRA process involves several steps, including normalizing process parameters to determine the gray relative coefficient (GRC) [17]. In In recent years, a network selection approach utilizing Gray System Theory has been investigated. This theory has proven effective in dealing with incomplete, uncertain, and limited data. Gray Relational Analysis, a fundamental aspect of Gray System Theory, is highly suitable for decision making involving complex interactions among various factors and variables.

While GRA has been effectively utilized for network selection, it is affected by the rank inversion problem. This paper offers a solution to resolve rank conflict in a GRA-based network selection algorithm. By thoroughly analysing the algorithm, we identify the root cause of rank reversal and explore ways to mitigate its impact. Our findings indicate that changing the normalization method can significantly reduce or eliminate rank reversals. To verify Based on our theoretical assumptions, we assessed the performance of the proposed solutions. Gray structure theory is used to assess the quality of the correlation between several distinct sequences and to identify the most suitable one. A reference sequence is designated to represent the best case.

The gray correlation is calculated based on the comparison between the reference sequence and other sequences on similarity and variance. This approach is also very applicable to network selection [18]. Gray correlation analysis is a crucial element of gray system theory, which addresses uncertainty in information. A system is classified as a white system if all information is known, a black system if no information is available, and a gray system if only partial information is known. Considering the multiple criteria involved in modelling the handover issue within a dense small cell environment, GRA serves as a powerful multi-attribute decision-making technique for addressing the cell selection issue. To assess the gray relationship between the handover metrics (attributes), gray correlation coefficients are calculated. The suggested method integrates the Analytical Hierarchy Process with Gray Correlation Analysis (GRA), where AHP Initially assigns weights to all HO metrics, followed by the application of GRA ranks neighbouring candidate cells to select the optimal HO target.Rank abnormality refers to the problem of inverse ranking, in which the order of alternatives changes when the lowest ranked option is removed. This leads to excessive redundant assignments (HOs). To address this, the proposed GRA-HO method incorporates an improved max-min normalization technique [19]. In addition, we extend these findings to the interval-valued context, and propose a modified The GRA method for multi-attribute decision-making using interval-valued data attributes and incomplete weight information.The GRA process begins by converting the performance of all alternatives is transformed into comparison sequences, a process known as gray relationship generation. Based on for these sequences, an ideal target sequence is established. Then, the gray relationship coefficients between each comparison sequence and the ideal target sequence are computed. In the final step, the gray relationship degree is determined for each alternative.

The alternative with the highest gray relationship degree with the ideal target sequence is considered the optimal choice [20]. Gray relational analysis (GRA) evaluates the similarity and compactness of different sequences based on their geometric shapes, while providing useful properties such as normalization and proximity. By assessing similarity and compactness, GRA effectively assesses the relationship between the collected evidence and identifies any underlying inconsistencies.Therefore, we introduce a novel conflict reallocation approach to pre-process and reallocate conflicts between the obtained evidence. This method aims to mitigate conflicts before applying Dumpster's addition rule by integrating gray relational analysis with the collected conflicting evidence. Gray relational analysis (GRA), a component of Gray systems theory, is well suited to solving problems involving complex interactions between multiple factors and variables. It solves the challenges of multi-criteria decision making (MCDM) by integrating all Combine the performance attribute values for each alternative into a single measure called the Gray relational rank. Unlike other MCDM methods that use multi-dimensional criteria for single-dimensional alternatives, GRA integrates multi-dimensional criteria across multiple alternatives. In addition, it considers the combined effect of two domains on a ranked pair instead of focusing on a single domain [21, 22].

As a project approved by the primary route was chosen by Pars Consulting Engineers, under the Ministry of Roads and Urban Development, while Omran Tatbir Kushan Consulting Engineers proposed three alternative routes. To evaluate and determine the optimal route, novel multi-attribute decision-making (MADM) methods were used. A comprehensive review of various studies was conducted to develop the evaluation framework, which led to an initial list of indicators. Subsequently, several meetings were held with the Expert Group on Road Construction and Urban Development, where the main indicators were determined based on expert assessments of their frequency and importance. A total of 35 indicators were chosen for route optimization. Using By incorporating expert opinions and the Dynamic Fuzzy GRA

method, each indicator was assigned a weight, leading to the identification of the optimal route among the four candidates.A literature review is conducted to establish an initial a set of evaluation criteria for the optimal path variants. The methodology of dynamic fuzzy GRA is then explained. Following this, a sample case study is presented, outlining the criteria weighting and the selection of the optimal. path variant. Finally, the main conclusions are presented with recommendations for future research [23]. Most industrial force measurements currently rely on Strain gauge-based load cells, with one end attached to a rigid structure, while the other supports the load.

These Load cells are commonly used as mass or force transducers in both static and dynamic weighing systems. In particular, heavy industry demands Load cells that are lightweight, durable, and capable of withstanding environmental conditions. To meet these requirements, advanced optimization methods are being developed using numerical simulation techniques. These discoveries will lead to improvements in existing products, significantly improve finite element analysis calculations and numerical simulations, and enable more efficient and effective computer-based approaches.Load cells measure force or weight under varying load and environmental conditions. Their accuracy is represented as a percentage of the overall capacity. Strain gauges fixed to particular parts of an elastic body serve a key role in generating a proportional output based on the applied force. When designing a load cell, factors like mass, pressure, and strain must be carefully considered. Depending on the weighing system, load cells can be used individually or in multiple combinations. These devices convert force or weight into an electrical signal for measurement and analysis [24]. It contains a large amount of known, unknown and unverified information, which is referred to as a gray system due to its limited, incomplete and uncertain data.

This concept was introduced by Deng Zhulong in 1982. Research in this field primarily includes gray system modelling theory, gray system control linkage theory, gray relational analysis (GRA), gray forecasting methods, gray planning methods and gray decision making methods.When analysing a system, it is necessary to distinguish between primary and secondary factors that positively or negatively influence its development. However, with incomplete and uncertain information, it can be challenging to determine the relationships between all factors and distinguish their importance in a gray system. The primary role of gray relationship analysis (GRA) is to evaluate and rank these factors to facilitate system analysis [25]. Taguchi-based experimental design is widely used by researchers for process optimization. Various authors have applied this approach to Single-objective optimization in the PCM process. Taguchi-based gray correlation analysis, a multi-objective optimization method, is employed to refine selected process parameters. In this method, multi-response Optimization issues are converted into single-response optimization problems by maximizing the overall gray correlation quality (GRG). Gray correlation the theory has been utilized across various fields, including agriculture, economics, industry, civil engineering, and manufacturing. David et al. explored the properties of water-based ferric chloride etchant employed in industrial photochemical machining, identifying $FeCl_3$ as a universal etchant for nearly all metals. Raj Kumar et al. examined the cost model for PCM, outlining various etchant standards and methods for their analysis and monitoring. Sagir simultaneously conducted a study on copper etching using $CuCl_2$ and the effective regeneration of waste etchant. The regeneration process not only reduces overall production costs, but also promotes an environmentally friendly etchant system, improving productivity [26].

The Gray Correlation Analysis method, a component of Gray System Theory, estimates the size of a system by analysing the correlation coefficients between various factors in the system. In this paper, we have developed an early warning system for banks by integrating GRA, banking sector ratings, and four major risk categories. The GRA method is often used for prediction because it provides higher accuracy compared to exact mathematical methods.Li Feng, Yu Hongtao, and FeiXiaoxia state that GRA "transforms the scope into conceptualization and modelling." As a result, GRA is increasingly used in a variety of fields, including social sciences, economics, engineering, technology, agriculture, industry, transportation, meteorology, environmental studies, hydrology, finance, medicine, and military. Recent research using GRA has focused on areas such as project risk assessment, risk measurement in the banking industry, the relationship between energy consumption and GDP, and data content analysis [27]. For efficient tooling, it is essential to select appropriate parameters to ensure the development of accurate PCM process and functional device.

This study focuses On response variables like undercut and surface roughness, using touch-based GRA to optimize process parameters. The research aims to provide a comprehensive analysis in this area.Gray correlation analysis, a key feature of gray system theory, evaluates the relationship between various factors by analysing correlation coefficients. In this study, the GRA technique was used to develop a banking early warning system, emphasizing banking sector assessments and four major risk categories. GRA is widely used for predictive analysis due to its strong mathematical foundations, providing higher accuracy than other methods [28]. General correlation analysis (GRA) is a widely used method for establishing correlation structures, assessing relationships within complete data sets, and identifying similarities or differences. Introduced by Huang and Lee in 2006, this approach measures variations, highlighting key factors within a given domain.Evaluating the influence of process variables on gray correlation formation involves the use of analysis of variance (ANOVA) techniques. Based on recent research, this includes examining factors such as casting wall thickness and its associated microstructure. The current study focuses on ductile iron casting, emphasizing the primary effects of various parameters and their impact on material properties [29].

Analysis and Discussion

Table 1: The drug list analysed using the GRA method

	Completeness	Accuracy	Efficacy	Applicability
Rifampicin	4.00	2.00	1.00	7.00
Isoniazid	5.00	3.00	8.00	8.00
Levofloxacin	8.00	6.00	11.00	4.00
Moxifloxacin	9.00	5.00	10.00	2.00
Etambutal	10.00	4.00	9.00	2.00

The drug list analysed using the GRA method, Table 1, Presents the performance of different TB treatments based on completeness, accuracy, efficacy, and compatibility. Rifampicin scored highest in compatibility (7.00) but had the lowest efficacy (1.00). Isoniazid showed consistent performance, excelling in efficacy (8.00) and compatibility (8.00). Levofloxacin and moxifloxacin showed the highest efficacy (11.00 and 10.00, respectively), although their compatibility was low (4.00 and 2.00). Ethambutol ranked highest in completeness (10.00) but shared the lowest compatibility with moxifloxacin (2.00). These findings underscore the need for careful selection of drugs, ensuring optimal interaction based on clinical needs.

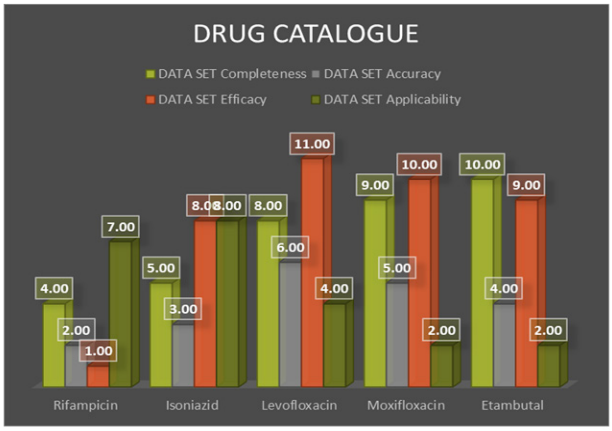

Figure 1 : Fraud Detection in Shipping Payments Using ML

Figure 1 illustrates the interaction of tuberculosis drugs using the GRA method. Rifampicin shows the highest compatibility (7.00) but the lowest efficacy (1.00). Isoniazid is balanced in efficacy (8.00) and compatibility (8.00). Levofloxacin and moxifloxacin excel in efficacy (11.00 and 10.00) but have the lowest compatibility. Ethambutol ranks highest in completeness (10.00).

Table 2: presents normalized data using the GRA method, which highlights the interoperability of TB drugs across four parameters

	Completeness	Accuracy	Efficacy	Applicability
Rifampicin	0.0000	0.0000	1.0000	0.1667
Isoniazid	0.1667	0.2500	0.3000	0.0000
Levofloxacin	0.6667	1.0000	0.0000	0.6667
Moxifloxacin	0.8333	0.7500	0.1000	1.0000
Etambutal	1.0000	0.5000	0.2000	1.0000

Table 2 presents normalized data using the GRA method, which highlights the interoperability of TB drugs across four parameters. Rifampicin achieves the highest efficiency (1.0000), but scores the lowest in completeness and accuracy (0.0000). Isoniazid shows moderate efficiency in accuracy (0.2500) and efficacy (0.3000), but no compatibility (0.0000). Levofloxacin leads in accuracy (1.0000), but has the lowest compatibility (0.0000). Moxifloxacin and ethambutol demonstrate the strongest completeness (0.8333 and 1.0000, respectively) and compatibility (1.0000), although their effectiveness remains limited. These results emphasize the importance of choosing drugs that work effectively based on treatment priorities and clinical conditions

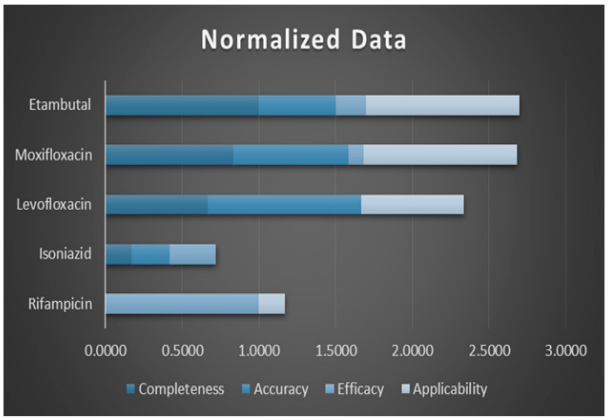

Figure 2 : Normalized data

Figure 2 presents the normalized data using the GRA method, which illustrates drug interactions. Rifampicin achieves the highest efficiency (1.0000), but has the lowest completeness and precision. Levofloxacin excels in precision (1.0000), but has the lowest efficiency (0.0000). Moxifloxacin and ethambutol scored highest in compatibility (1.0000), highlighting their differing strengths in TB treatment selection.

Table 3. Deviation sequence

	Completeness	Accuracy	Efficacy	Applicability
Rifampicin	1.0000	1.0000	0.0000	0.8333
Isoniazid	0.8333	0.7500	0.7000	1.0000
Levofloxacin	0.3333	0.0000	1.0000	0.3333
Moxifloxacin	0.1667	0.2500	0.9000	0.0000

Etambutal	0.0000	0.5000	0.8000	0.0000

Table 3 presents the order of deviation using the GRA method, which reflects the interoperability of TB drugs. Rifampicin shows the highest deviation in completeness and accuracy (1.0000) but no deviation in efficacy (0.0000). Isoniazid shows moderate deviation in all parameters, the highest in compatibility (1.0000). Levofloxacin has the lowest precision deviation (0.0000) but the highest efficacy deviation (1.0000). Moxifloxacin and ethambutol show the lowest compatibility deviation (0.0000), indicating strong consistency in that aspect. These variations highlight how different drugs work in treatment, emphasizing the need for careful selection based on clinical goals and therapeutic balance.

Table 4. Grey Relation Coefficient

	Completeness	Accuracy	Efficacy	Applicability
Rifampicin	0.3333	0.3333	1.0000	0.3750
Isoniazid	0.3750	0.4000	0.4167	0.3333
Levofloxacin	0.6000	1.0000	0.3333	0.6000
Moxifloxacin	0.7500	0.6667	0.3571	1.0000
Etambutal	1.0000	0.5000	0.3846	1.0000

Table 4 presents the Gray Relationship Coefficient (GRA) method demonstrating the interaction of tuberculosis drugs. Rifampicin achieves the highest efficiency (1.0000), but the lowest completeness and precision (0.3333). Isoniazid maintains balanced coefficients, with the highest in efficiency (0.4167). Levofloxacin leads in precision (1.0000), but has the lowest efficiency (0.3333). Moxifloxacin and ethambutol excel in compatibility (1.0000), with ethambutol also having the highest completeness (1.0000). These coefficients indicate how well each drug correlates across multiple parameters, guiding optimal drug selection based on therapeutic efficacy and adaptability in different clinical situations.

Table 5. Final GRG ranking result

	GRG	Rank
Rifampicin	0.5104	4
Isoniazid	0.3813	5
Levofloxacin	0.6333	3
Moxifloxacin	0.6935	2
Etambutal	0.7212	1

Table 5 presents the final Gray Relation Grade (GRG) ranking, which highlights the interoperability of TB drugs based on the GRA method. Ethambutol achieves the highest GRG score (0.7212), earning the first rank due to its strong overall efficacy. Moxifloxacin follows closely (0.6935), indicating high compatibility. Levofloxacin is in third place (0.6333), showing balanced properties. Rifampicin (0.5104) and isoniazid (0.3813) reflect their limited interoperability in some aspects. These rankings emphasize the varying effectiveness of each drug, aiding in informed clinical decision-making to optimize treatment strategies based on specific treatment needs and patient conditions.

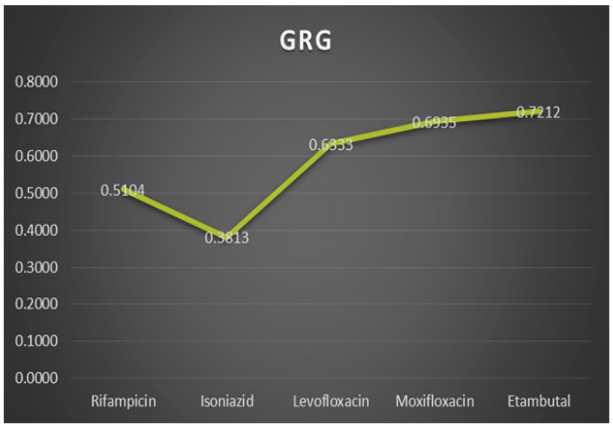

Figure 3 : illustrates the final Gray Relation Grade (GRG) ranking

Figure 3 illustrates the final Gray Relation Grade (GRG) ranking, which demonstrates the interoperability of TB drugs using the GRA method. Ethambutol achieves the highest GRG score (0.7212), indicating excellent overall performance. It is followed by moxifloxacin (0.6935), reflecting strong compatibility. Levofloxacin (0.6333) is in third place, showing consistent properties. Rifampicin (0.5104) and isoniazid (0.3813) have low GRG scores, indicating limited interoperability in some parameters. These rankings provide valuable insights for selecting optimal drug combinations, ensuring effective treatment strategies. By assessing GRG scores, clinicians can prioritize drugs that best align with treatment objectives and patient-specific needs in TB management.

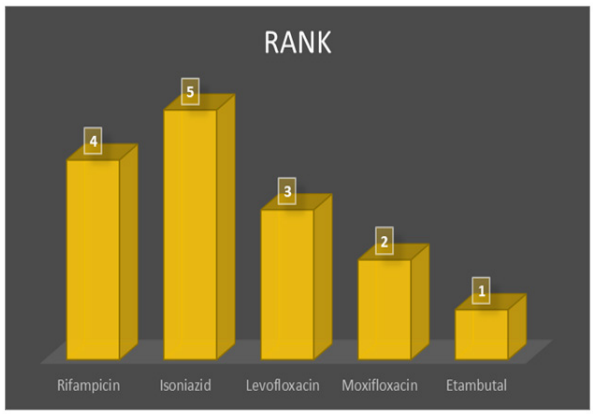

Figure 4: Ranking displayed

Figure 4, final GRG ranking, which highlights drug interactions using the GRA method. Ethambutol ranks highest (1), followed by moxifloxacin (2) and levofloxacin (3), indicating excellent efficacy. Rifampicin (4) and isoniazid (5) rank lowest, indicating limited compatibility. These rankings help to improve TB treatment selection.

Conclusion

This study employed The Gray Relational Analysis method is used to assess the interoperability of tuberculosis (TB) drugs across four critical parameters: completeness, accuracy, efficacy, and applicability. The findings reveal significant variations in how these drugs perform across multiple dimensions, highlighting the complexity of TB treatment selection. Ethambutol emerged as the optimal drug with the highest Gray Relational Grade (GRG) of 0.7212, indicating superior overall performance across the evaluated parameters. This was followed by moxifloxacin (0.6935) and levofloxacin (0.6333), both demonstrating strong compatibility and balanced properties. Rifampicin and isoniazid ranked lowest with GRG scores of 0.5104 and 0.3813 respectively, reflecting their limitations in certain aspects despite their historical importance in TB treatment regimens.

The analysis demonstrates that while some drugs excel in specific parameters such as rifampicin's high efficacy (1.000) but low completeness and accuracy (0.3333) they may underperform in others. These trade-offs emphasize the importance of taking a holistic approach to TB treatment, where drug selection must be guided by comprehensive evaluation rather than single-parameter optimization. The GRA method proves valuable in providing a systematic framework for comparing drug performances across multiple dimensions simultaneously. By transforming complex multi-objective problems into single-objective optimization, it offers clinicians a practical tool for informed decision-making in TB management. These findings contribute to the ongoing effort to optimize TB treatment strategies, particularly in regions with diverse and complex drug resistance patterns. The significant variance in drug performance across parameters suggests that personalized treatment approaches, tailored to patient-specific needs and conditions, and may be more effective than standardized protocols. Future research should expand this analysis to include more TB drugs and additional parameters, further refining our understanding of drug interoperability to enhance treatment outcomes in tuberculosis management.

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