German J Pharm Biomaterials 2024; 3(3): 9-17
https://doi.org/10.5530/gjpb.2024.3.8

GJPB

Research Article

Statistical analysis of the critical quality attributes of 1,2-dihydroxypropane as a pharmaceutical excipient

Mostafa Essam Ahmed Mostafa Eissa

Department of Pharmaceutical SPC, Pharmaceutical and Medicinal Research Facility, Cairo, Egypt.

*Correspondence: mostafaessameiss@yahoo.com

Received: 19 January 2024; Revised: 09 March 2024; Accepted: 19 March 2024

Abstract

The constituting ingredients, either active or inactive, directly influence the quality and efficacy of the pharmaceutical medicinal product. One of the most common and versatile excipients used in various industries, including pharmaceuticals, is 1,2-propanediol, propylene glycol, or methyl ethyl glycol. The present work aims to trend the quality characteristics of Methyl ethyl glycol using exploratory process-behavior plots, which are graphical tools for monitoring and improving process performance. This study focused on the assay and water content tests of the initial 34 batches of the manufactured 1,2-Propanediol using a standard analysis method according to the British Pharmacopoeia (BP), which specifies this excipient's quality requirements and limits. Exploratory Shewhart charts, the simplest and most widely used control charts, were plotted using Statistical Process Control (SPC) software. The results showed that the data did not follow a normal distribution, and there were several out-of-control signals from both quality aspects, indicating that the process was unstable and unpredictable even if no results exceeded the specifications criteria. The study suggests that the supplier needs to improve the process control and the quality limits of Methylethylene glycol to ensure its consistency and reliability. The application of SPC techniques is essential for the modern, competitive chemical industry, as they help to reduce variability, enhance quality, and optimize resources. Trending charts provide a quantitative estimation of the current situation and the actions needed for the future improvement of the quality control tests. Future research could explore the impact of the quality variation of 1,2-Propanediol on the performance and stability of the final dosage forms, as well as the potential risks and benefits of using alternative excipients with similar properties.

Keywords: Normal distribution; out-of-control; statistical process control; trending chart; Propane-1,2-diol

Introduction

Statistical Process Control (SPC) is a quality control technique that uses statistical methods to monitor and control the inspection characteristics of products or processes. Inspection characteristics are the features that are measured and inspected to verify that they meet the specification limits [1]. SPC is widely used in the manufacturing industry, especially in the chemical and pharmaceutical sectors, where the quality and consistency of the products are vital for the safety and efficacy of the medication [2-5]. SPC provides a systematic approach to process control by analyzing data and identifying process variations that can affect the quality of the products [6]. SPC also helps improve product quality and customer satisfaction by reducing defects, rework, and costs.

SPC's main principles and tools include defining the critical process parameters, collecting and analyzing data, and using control charts and process capability analysis to monitor and control the process [7]. Control charts are graphical tools that display the process performance over time and detect any out-of-control signals that indicate process instability or unpredictability [8]. Process capability analysis is a statistical tool that evaluates the ability of the process to meet the specification limits and indicates the potential for improvement.

SPC has been applied in various fields and industries to monitor and control inspection characteristics and improve quality control [9]. Other studies showed that SPC has proven to be effective in reducing defects, improving process efficiency, and increasing customer satisfaction [8]. However, the previous studies also reveal some limitations and gaps in the current research, such as the need for more empirical studies and the need to explore the application of SPC in different industries and analyses [9]. It is crucial that future research addresses these limitations and gaps, as this will provide a more comprehensive understanding of the role of SPC in improving quality control in manufacturing.

While SPC's effectiveness in reducing defects and improving quality is well documented [8,9], previous research also highlights limitations [9]. More empirical studies are needed to explore SPC implementation in under-researched industries, such as chemical industries of medicinal compounds. Additionally, research on integrating advanced data analysis techniques with SPC could offer a more comprehensive understanding of its role in quality control.

Propylene glycol, also known as 1,2-dihydroxypropane, functions as a crucial pharmaceutical excipient. Excipients are inactive ingredients that play essential roles in delivering drugs effectively. In the case of propylene glycol, it serves as a solvent, humectant, and plasticizer in various pharmaceutical formulations [10]. These functionalities directly impact medications' stability, shelf life, and efficacy. Even minor variations in the purity of propylene glycol can significantly affect drug performance, potentially leading to reduced effectiveness or even adverse reactions.

To ensure patient safety and drug efficacy, strict regulations govern the quality control of pharmaceutical excipients. Regulatory bodies like the United States Pharmacopeia (USP) and European Pharmacopoeia (Ph. Eur.) set forth specific quality standards for propylene glycol, including limits for assay (purity) and water content. Manufacturers must adhere to these stringent requirements to guarantee the quality and safety of their products. Statistical Process Control (SPC) is a powerful tool for pharmaceutical manufacturers to produce high-quality propylene glycol consistently. By continuously monitoring the critical quality attributes (CQAs) of assay and water content through control charts, SPC enables [7,8] **Early detection of deviations:** SPC charts can identify trends or unusual variations in the assay or water content before they reach critical levels. This allows for prompt intervention and corrective actions, preventing the production of non-conforming batches. **Improved process consistency:** SPC helps pinpoint and address assignable causes of variation in the manufacturing process. By minimizing these variations, manufacturers can achieve greater consistency, ensuring that every batch of propylene glycol meets the required quality specifications. **Reduced risk of product failures:** Early detection of potential issues through SPC allows corrective actions to be taken promptly. This minimizes the risk of producing batches that fail quality-control tests and potentially need to be discarded, leading to significant time and resource losses.

This research paper presents a case study of propylene glycol, a common pharmaceutical excipient, and two of its quality control tests that use trending charts in the chemical pharmaceutical industry. The paper will analyze quality control data from previous batches and apply SPC to monitor and control inspection characteristics. The paper will then report SPC's main findings and insights, including control charts and data patterns. Finally, the paper will justify the research objective and scope in the context of the pharmaceutical-grade excipient compound model in the chemical industry.

Materials and Methods

Materials

A new pharmaceutical-grade raw material from an Asian chemical manufacturer was imported. The market retailer provided samples of propylene glycol or α-propylene glycol (propane-1,2-diol in IUPAC) from sequential batches [10]. 1,2-dihydroxypropane which is colorless and odorless liquid with molecular formula CH3CH(OH)CH2OH has a molar mass of 76.095 $g \cdot mol^{-1}$. The raw chemical compound was analyzed using standard methods of the official compendia for the assay and water content [11,12]. Quality datasets of the testing were collected and stored in an electronic storage database.

Methods

The data analysis and visualization were performed using Statistical Process Control (SPC) techniques. Following the general approach for exploratory purposes, process-behavior charts, also known as control charts, were created [3,13]. The data first underwent normality testing using the Anderson-Darling (AD) test at a 95% confidence interval (CI) and α 0.05 [14,15]. If the data exhibited a non-normal distribution, normalization techniques were applied using either the Johnson family of transformations or the Box-Cox transformation, depending on the data characteristics [15,16]. These transformations mathematically modify the data to achieve a more symmetrical and normal distribution, making it suitable for control chart analysis. In cases where the data could not be normalized using these techniques, the capability analysis was excluded [15]. Software like Minitab can be utilized for these analyses and control chart generation.

Data analysis and visualization

The data analysis and visualization were performed using Statistical Process Control (SPC) techniques. SPC is a quality control technique that uses statistical methods to monitor and control the inspection characteristics of products or processes [13]. The steps of the data analysis and visualization for the assay and water content tests were as follows [14-16]:

- The distribution of the data was identified at a 95% confidence interval (CI) and α 0.05 using the Anderson-Darling (AD) method [15,16]. The AD method is a statistical test that evaluates how well the data fit a certain distribution.
- The Johnson family or Box-Cox transformation techniques were used to normalize the raw data, which did not follow any clear trend [9]. These mathematical methods transform the data to make them more symmetric and normal-like.
- The capability analysis was excluded if the data did not fit any definite distribution even after the transformation [15]. Capability analysis is a statistical tool that evaluates the ability of the process to meet the specification limits and indicates the potential for improvement.
- The process-behavior charts were created using the general approach for exploratory purposes [3]. Process-behavior charts, also known as control charts, are graphical tools that display the process performance over time and detect any out-of-control signals that indicate process instability or unpredictability.
- The control limits and the specification limits for each test were meticulously compared and investigated. The control limits are the boundaries of the natural variation of the process, while the specification limits are the requirements or standards for the product or process quality. The comparison and investigation were thorough, aiming to identify any abnormal patterns or sources of variation that could affect the quality of the product.

Results and Discussion

Propylene glycol is a diol with a sweet taste and a colorless and odorless appearance [11]. It can mix well with many solvents, such as water, acetone, and chloroform, and has a high boiling point of 188.2 °C [12]. It is widely used in the manufacture of polymers and as a humectant, emulsifier, and preservative in various sectors, such as food, cosmetics, pharmaceuticals, and electronics [13]. It is generally considered safe for specific uses by the US FDA and the EU, but it may cause harm to some people or animals if consumed or exposed excessively [14].

Quality is crucial in the manufacturing industry, and various methods and tools are required to ensure and maintain it [15]. One of these tools is Statistical Process Control (SPC), a statistical technique that helps to analyze and control processes [16]. SPC is especially useful in manufacturing chemical compounds, as it can verify that the final product conforms to the specifications [17,18]. SPC can monitor two essential parameters of chemical compounds: water content and assay. The water content is the amount in a compound, measured as a percentage. The assay is the percentage of the active ingredient in a compound, measured quantitatively [11,12]. Control charts are indispensable for monitoring and

controlling the water content and assay of chemical compounds [19]. A Shewhart chart is a control chart that plots process data over time to detect any variation or deviation from the target [20]. In this case, the control limits of the water content and assay results were based on the standard reference.

Distribution identification for assay

The test is about finding the distribution type for the assay data (Table 1). Minitab®v17.1.0 tries different distribution types and gives some notes and warnings [21]. The first part of the test says that a Johnson transformation function is not used because the p-value is more than 0.1. This means that the data are close to normal without transformation [22]. The second part of the test says that a 2-parameter exponential distribution has a warning about the variance/covariance matrix of the estimated parameters. This means that the parameter estimates may not be good, which can make the confidence intervals wrong [21]. The third part of the test says that a 3-parameter Weibull distribution has alarms about the algorithm's convergence and log-likelihood criterion.

Table 1. Distribution fit results for assay of propylene glycol.

Distribution	Location	Shape	Scale	Threshold	AD	P	LRT P
Normal	99.83824		0.24620		3.777	<0.005	
Lognormal	4.60355		0.00247		3.780	<0.005	
2-Parameter Exponential			0.86364	98.97460	9.013	<0.010	0.000
3-Parameter Weibull		3.60577E+05	50689.13304	-5.05892E+04	4.111	<0.005	0.772
Gamma		1.68968E+05	0.00059		3.815	<0.005	
3-Parameter Gamma		24104.01042	0.00157	61.66851	50.215	*	1.000

- Pooled sample is obtained from each batch manufactured lot of the raw chemical compound after manufacturing.
- The table only includes the distributions that have a P-value less than 0.01 for the Anderson-Darling (AD) test, which measures how well the data fit the distribution.
- The table also includes the likelihood ratio test (LRT) P-value for the distributions that have an extra parameter (threshold), which measures how much the extra parameter improves the fit.
- The table is sorted by the AD P-value in ascending order, so the distributions with the lowest P-value are at the top.
- The table uses scientific notation (E) for very large or small numbers, such as 3.60577E+05, which means 3.60577 x 10^5.
- The table uses an asterisk (*) to indicate that the P-value is not available or not applicable.

These alarms mean that the algorithm cannot find the best parameter estimates, which can be because the data do not fit the distribution or the starting parameter values are wrong. Also, the variance/covariance matrix of the estimated parameters does not exist, which can make the confidence intervals wrong. The last part of the test says that a 3-parameter Gamma distribution has the same alarms as the Weibull distribution [21]. These alarms mean that the parameter estimates may not be reasonable, and the confidence intervals may not be correct. The test also gives the goodness-of-fit test results for different distributions and the maximum likelihood estimates of the distribution parameters. The descriptive statistics and Box-Cox transformation are also given for the data [22]. The test shows that the data do not match well with any distribution type.

Distribution identification for water content

Minitab®v17.1.0 results show the distribution type for the water content (Table 2). The data have zero or negative values, so some distribution types, such as Exponential, Lognormal, Weibull, Gamma, and Log logistic, cannot be used. Also, Box-Cox transformation cannot be done because of the zero or negative values [22]. The Johnson transformation function cannot be chosen because the P-value is more than 0.1, so no transformation is done [21]. Three-parameter Lognormal, three-parameter Weibull, three-parameter Gamma, and three-parameter Log logistic distributions cannot make the variance/covariance matrix of estimated parameters, so the threshold parameter is fixed when finding confidence intervals.

Minitab® v17.1.0 also gives the Maximum Likelihood (ML) estimates of distribution parameters for each distribution type. ML estimates of distribution parameters are the values of the parameters that make the distribution model fit the data best [21]. They are found using a method called maximum likelihood, which tries to maximize the probability of the data given the model. The goodness of fit test

shows that the normal and logistic distributions have the smallest AD P-values. In contrast, the three-parameter Lognormal and three-parameter Gamma distributions have the biggest AD P-values. This means that the data do not match well with any distribution type.

Table 2. Distribution fit results for water content of propylene glycol.

Distribution	Location	Shape	Scale	Threshold	AD	P
Normal	0.02206		0.02129		1.210	<0.005
Logistic	0.02038		0.01202		1.152	<0.005
Largest Extreme Value	0.01244		0.01595		1.407	<0.010
Smallest Extreme Value	0.03327		0.02395		1.808	<0.010
2-Parameter Exponential			0.02273	-0.00067	4.816	<0.010
3-Parameter Weibull		0.29207	0.00825	-0.00000	5.691	<0.005
3-Parameter Loglogistic	-7.13290		4.01357	-0.00000	5.505	*
3-Parameter Lognormal	-14.07563		15.19920	-0.00000	6.606	*
3-Parameter Gamma		0.08116	0.27181	-0.00000	10.253	*

- Pooled sample is obtained from each batch manufactured lot of the raw chemical compound after manufacturing.
- The table only includes the distributions that can be fitted to the data, as some distributions cannot be used because the data contain non-positive values.
- The table is sorted by the Anderson-Darling (AD) statistic in ascending order, so the distributions with the lowest AD statistic are at the top.
- The table uses scientific notation (E) for very large or small numbers, such as 0.29207E+05, which means 0.29207 x 105.
- The table uses an asterisk (*) to indicate that the P-value is not available or not applicable.

Trending charts examination of inspection aspects

The following analysis shows the test results for modified U charts and the conventional Individual (I) charts created using Minitab software in Figures 1 and 2. The tests check the stability of the process-behavior chart for assay and moisture content [23]. The test results show the points that cross the control limits of the chart. These points are signals that the process is out of control. The processes are unstable and have variations. The users should examine the points that failed the tests and find the causes of the problems. The users should take action to fix the problems and make the process stable and quality-oriented.

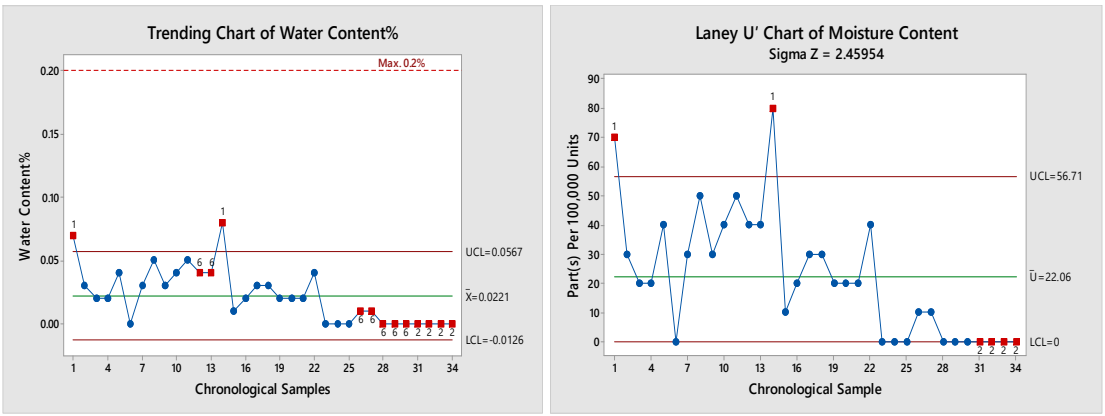

Figure 1. Process-behavior plot of the water content test for 1,2-Dihydroxypropane 34 chronological samples showing out-of-control points, the mean (X), Upper Control Limit (UCL) and Lower Control Limit (LCL).

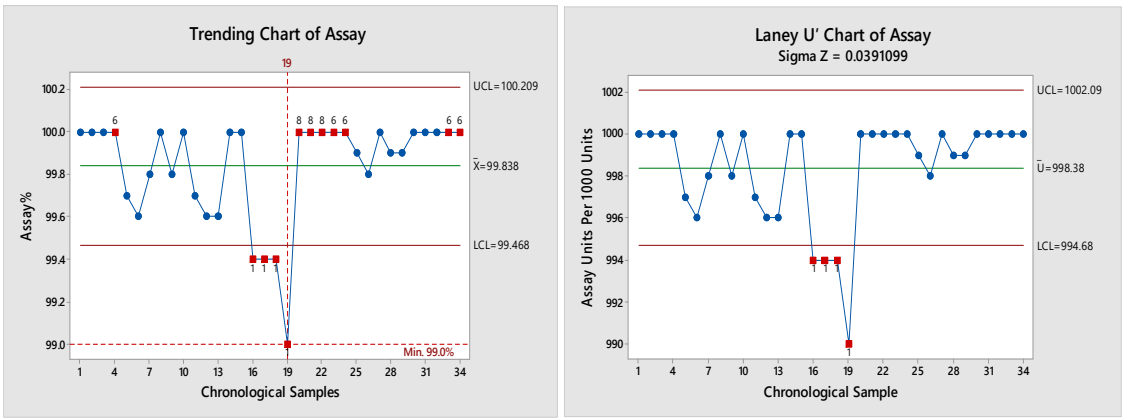

Figure 2. Process-behavior plot of the assay test for 1,2-Dihydroxypropane 34 chronological samples showing out-of-control points, the mean (X), Upper Control Limit (UCL) and Lower Control Limit (LCL).

Trending chart of inspection characteristics of the raw chemical material

Essential information about the control charts for the assay of 1,2-Dihydroxypropane:

- *I-Chart of assay:*
  - This chart shows the individual values of the assay over 34 batches.
  - The center line is the average of the assay values, which is 99.84%.
  - The upper control limit (UCL) is 100.209%, and the lower control limit (LCL) is 99.468%, calculated using the average moving range method.
  - There are four points that fall below the LCL, indicating a possible out-of-control condition in the process.
- *Laney U' Chart of assay:*
  - This chart shows the standardized units per thousand of the assay over 34 batches.
  - The center line is the average of the standardized units, which is 998.38.
  - The UCL is 1002.09, and the LCL is 994.68, calculated using the Laney method, which adjusts for under-dispersion in the data.
  - Four points also fall below the LCL, indicating a possible out-of-control condition in the process.
- *Comparison and conclusion:*
  - Both charts show similar trends and identify the same out-of-control points, batches between 16 and 19.
  - These batches have significantly lower assay values than the rest of the data, suggesting a problem in the process or measurement system.
  - The Laney U chart is more appropriate for this data, as it accounts for the non-normal distribution and the data's over- or under-dispersion.
  - The process needs to be investigated and improved to ensure the quality and consistency of the assay.
  - Key information about the control charts for the water content of 1,2-Dihydroxypropane.
- *I-Chart of water content*

  This chart shows the individual values of the water content over 34 batches. The center line is the average of the water content values, which is 0.0221%. The upper control limit (UCL) is 0.0567%, and the lower control limit (LCL) is -0.0126%, calculated using the average moving range method. Several points exceed the UCL, indicating variability in the process. While this might seem like an error, it can occur due to the nature of the control chart calculation procedure, specifically when using it for inherently positive data like percentages. In such cases, the negative LCL should be set to 0%, as a percentage cannot be negative. Several points exceed the UCL, indicating assignable cause(s) of variability in the process.
- *Laney U' chart of water content*

  This chart shows the standardized units per thousand water content over 34 batches. The center line is the average of the standardized units, which is 22.06. The UCL is 56.71, and the LCL is 00.00, calculated using the Laney method, which adjusts for over-dispersion in the data. A significant spike around batches 1 and 14 exceeds the UCL, indicating an anomaly or outlier in the data.
- *Comparison*

  Given that no distinct distribution could be identified due to the non-normal distribution of assay results, both charts might offer insights. However, the Laney approach might be preferable as it is designed for data that does not follow a normal distribution. Both charts show variability prominently. The process needs to be investigated and improved to ensure the quality and consistency of the water content.

Water content

Test 1: One point more than 3.00 standard deviations from center line. This test checks if any data point is more than 3.00 standard deviations away from the centerline. As per the given results, this test has failed at points 1 and 14. **Test 2:** 9 points in a row on the same side of the centerline. This test checks

if nine consecutive data points are above or below the centerline [19]. As per the results, this test has failed at points 31, 32, 33, and 34. **Test 6:** 4 out of 5 points more than 1 standard deviation from center line (on one side of CL). Figure 1 describes the fining.

This test checks if four out of five consecutive data points are more than 1 standard deviation away from the centerline on one side. As per the given results, this test has failed at points 12, 13, 14, 26, 27, 28, 29, 30, 31, 32, 33, and 34. **Test 8:** 8 points in a row with more than 1 standard deviation from the center line (above and below CL) [19]. This test checks if eight consecutive data points are more than 1 standard deviation away from the centerline, either above or below the centerline. As per the given results, this test failed at points 29, 30, 31, 32, 33, and 34. Laney chart showed similar output but with fewer alarm types.

Assay

The first test performed is Test 1, which checks if any point exceeds 3.00 standard deviations from the centerline. The test failed at points 16, 17, 18, and 19, indicating that the process is out-of-control. The next test is Test 5, which checks if 2 out of 3 points are more than 2 standard deviations from the centerline on one side of the centerline. The test failed at points 17, 18, and 19, indicating that the process is unstable [19]. The third test is Test 6, which checks if 4 out of 5 points are more than 1 standard deviation from the centerline on one side of the centerline. The test failed at points 4, 19, 23, 24, 33, and 34, indicating that the process is unstable.

The final test is Test 8, which checks if 8 points in a row are more than 1 standard deviation from the centerline, above and below the centerline. The test failed at points 17, 18, 19, 20, 21, 22, 23, and 24, indicating that the process is not stable at these points. In summary, the results of the I Chart for Assay indicate that the process is not stable at multiple points. The tests performed have provided valuable information about the stability of the process, which can be used to identify and eliminate the causes of variation [19]. By doing so, the process can be improved, and the quality of the product can be increased. Again, the Laney-trending chart shows a similar pattern but with fewer varieties of alarming points. Control charts that show the output can be visualized in Figure 2 demonstrating two approaches that are almost equivalent with just a few differences in the alarms.

The assay and water content tests are essential for evaluating the quality and purity of propylene glycol, according to the British Pharmacopeia. These tests help detect any differences from the expected values, which may indicate impurities or variations in the composition of propylene glycol [24]. These impurities or variations can affect the safety and efficacy of propylene glycol in various applications, such as food, cosmetics, pharmaceuticals, and electronics [25]. Therefore, it is important to follow these standards and take corrective actions if needed. By keeping the assay and water content levels within the specified range, industries can ensure that their products meet the required standards and provide high-quality substances to consumers.

Using multiple control chart tests provides a more comprehensive picture of process stability. Focus beyond Random Variation: The 3 sigma test primarily identifies random variation inherent in any process. While necessary, it does not tell the whole story. Other tests can detect specific patterns in the data that might indicate special causes of variation, like shifts in the mean, trends, or recurring cycles. Targeted Detection: Different control chart tests have specific strengths. For example, the run test is sensitive to unusual patterns like points above or below the center line sequences. Reduced False Alarms: Relying solely on the 3 sigma test can sometimes lead to false alarms. If the data distribution is irregular, points outside the control limits might not necessarily indicate a problem. Additional tests can help confirm if these points indeed indicate a particular cause.

While using multiple alarm tests seems exhaustive, there are justifications for using multiple tests. Early Detection: Using a combination of control chart tests, the investigator can detect problems earlier. This allows for quicker intervention and minimizes potential product quality or process efficiency issues. Deeper Process Understanding: A more comprehensive range of tests provides a richer picture of process behavior. This helps identify specific types of variation and allows for more targeted adjustments to improve process stability. However, it is essential to consider other challenges. Balance:

While using multiple tests is beneficial, avoiding information overload is also essential. Choosing a focused set of tests relevant to the specific process and potential issues is critical. False Alarm Management: More tests increase the probability of encountering a false alarm. Having clear guidelines for interpreting chart signals and investigating potential issues becomes crucial. Using a combination of control chart tests offers a more comprehensive and nuanced view of process stability. This allows for earlier detection of problems and a deeper understanding of process behavior, ultimately leading to better process control and improved product quality.

SPC is a useful method for monitoring and controlling the assay and water content tests, especially in the manufacturing of propylene glycol [26]. By using control charts, such as the Laney and I-Charts, manufacturers can ensure that the assay and water content values are consistent and close to the target [27,28]. This improves the product quality and increases customer satisfaction [29,30]. As the manufacturing industry continues to develop, SPC will continue to be a valuable tool for maintaining quality standards and driving continuous improvement [31]. The I-Chart of the assay and water content tests is an effective tool for tracking the quality levels of propylene glycol. By performing various tests on the chart, manufacturers can identify and correct any deviations or patterns that may affect the quality of propylene glycol. SPC helps ensure that propylene glycol meets the desired quality standards, thus ensuring safety and efficacy in its applications.

Conclusion

The assay and moisture content tests are essential for evaluating the quality and purity of propylene glycol, which is used in various applications in the pharmaceutical chemical industry. SPC is a valuable quality control technique widely used in manufacturing to monitor and control these tests. SPC uses statistical methods to analyze data and detect variations in the process. By using SPC, manufacturers can improve the quality of propylene glycol, lower costs, and satisfy the customers. The existing studies on SPC in monitoring and controlling these tests show that SPC can improve process control and product quality. However, more research is needed to overcome the challenges and gaps in the current knowledge. Some challenges and gaps are related to the data distribution, which may not follow any known distribution type, such as the standard or Gaussian distribution. This can be because of the nature of the data, the outliers or extreme values, the small sample sizes, or the complex variables. The warnings in the distribution identification analysis show the difficulties and limitations of statistical modeling and the need for careful analysis and interpretation of the results.

Authors contribution

The work was done by a single contributing author.

Declaration of interest

The authors declare no conflict of interest.

Financial support

This work has not received any funds from national and international agencies.

References

1. Eissa M. Implementation of modified Q-control chart in monitoring of inspection characteristics with finite quantification sensitivity limits: A case study of bioburden enumeration in capsule shell. El-Cezeri. 2021;8(3):1093-1107.
2. Eissa M. Bioburden control in the biopharmaceutical industry. BioPharm International. 2017;24-27.
3. Eissa M, Mahmoud A, Nouby A. Evaluation and failure risk of microbiological air quality in production area of pharmaceutical plant. RGUHS J Pharm Sci. 2016;5:155-166.
4. Eissa M. Establishment of biocidal activity evaluation study protocol in healthcare facility for routine monitoring of antibacterial activity of disinfectants. J Exp Clin Med. 2022;39(4):939-947.
5. Eissa EM. Assessing the antimicrobial efficacy of eye drop products. Eur Pharm Rev. 2019.

6. Eissa MM. Quality criteria establishment for dissolution of ascorbic acid from sustained release pellets. Novel Tech Nutr Food Sci. 2018;2(2):137-142.
7. Eissa ME. Statistical process control and quantitative microbiological risk assessment combination in healthcare industry. Biomed Engg Biotech. 2018;2(1):14-17.
8. Eissa ME. Shewhart control chart in microbiological quality control of purified water and its use in quantitative risk evaluation. UK J Pharm Biosc. 2016;4(1):45-51.
9. Eissa M, Rashed E, Eissa DE. Quality improvement in routine inspection and control of healthcare products using statistical intervention of long-term data trend. Dicle Üniversitesi Fen Bilimleri Enstitüsü Dergisi. 2021;10(2):163-184.
10. Eissa M, Mahmoud A. Evaluation of microbial recovery from raw materials for pharmaceutical use. J Food Pharm Sci. 2016;4(1):6-11.
11. British Pharmacopoeia Commission. British pharmacopoeia 2023. TSO. 2023.
12. United States Pharmacopeial Convention. United States pharmacopeia and national formulary (USP 46–NF 41). U.S. Pharmacopeial Convention, Inc. 2023;Propylene Glycol Monograph.
13. Gao Y, Zhang Y, Zhang J, Wang X, Wang H, Li X. 1,2-Propanediol as a heat transfer fluid for medium-temperature solar thermal applications. Sol Energy. 2019;185:1-9.
14. Food and Drug Administration. 1,2-Propanediol. In: Food additives permitted for direct addition to food for human consumption. 21 CFR Part 184. U.S. Government Printing Office; 2019. p. 184.1666.
15. Eissa M. Statistical Process Control and Capability Six-pack for Conductivity Measurement in Medicinal Chemical Industry. J Pharmacol Pharm Res. 2024;1(1):9-14.
16. Eissa M, Rashed E, Eissa DE. Microbiological Stability Assessment of Municipal Distribution Line Using Control Chart Approach for Total Bioburden Count. Sağlık Akademisi Kastamonu. 2023;8(2):363-83.
17. Eissa ME. Novel rapid method in ecological risk assessment of air-borne bacteria in pharmaceutical facility. Mahidol Univ J Pharm Sci. 2016;43(3):115-126.
18. Eissa M. Evaluation of microbiological purified water trend using two types of control chart. Eur Pharm Rev. 2018;23(5):36-8.
19. Eissa ME, Seif M, Fares M. Assessment of purified water quality in pharmaceutical facility using six sigma tools. Int J Qual Assur. 2015;6(2):54-72.
20. Eissa ME, Mahmoud AM, Nouby AS. Control chart in microbiological cleaning efficacy of pharmaceutical facility. Dhaka Univ J Pharm Sci. 2016;14(2):133-138.
21. Lide DR, editor. CRC handbook of chemistry and physics. 94th ed. CRC Press; 2013. p. 3-274.
22. Johnson NL. Systems of frequency curves generated by methods of translation. Biometrika. 1949;36(1-2):149-76.
23. Eissa ME. Variable and attribute control charts in trend analysis of active pharmaceutical components: Process efficiency monitoring and comparative study. Exp Med. 2018;1(1):32-44.
24. USP Monographs: Propylene Glycol. USP–NF. 2010;1-3. [Cited 2024 August 06]. Available at: https://www.uspnf.com/sites/default/files/usp_pdf/EN/USPNF/propyleneGlycol.pdf
25. E59 - PROPYLENE GLYCOL. PMDA. 2016;1-4. [Cited 2024 August 06]. Available at: https://www.pmda.go.jp/files/000199137.pdf
26. Standard test methods for analysis of ethylene glycols and propylene glycols. ASTM. 2002;1-15. [Cited 2024 August 06]. Available at: https://www.kelid1.ir/FilesUp/ASTM_STANDARS_971222/E202.PDF
27. Rashed ER, Eissa ME. Long-term quantitative assessment of women survivability from cancer: A unique descriptive analysis. Highlights Biosci. 2020;3:1-8.
28. Rashed ER, Eissa ME. Long-term monitoring of cancer mortality rates in USA: A descriptive analysis using statistical process control tools. Iberoam J Med. 2020;2(2):55-60.
29. Eissa ME, Rashed ER. Analysis and modeling of morbidity and mortality from coronavirus outbreak in Brazil: A case study of public health challenge using unique statistical tools. J Health Sci Res. 2020;8(2):57-61.
30. Eissa M. SPC and evaluation of analyst performance. Pharma Focus Asia. 2020.
31. Eissa ME, Hamed HS. Application of statistical quality control tools for monitoring of pharmaceutical product properties: SISPQ, GxP, pharmaceutical product, drug properties. Biol Sci-PJSIR. 2019;62(1):39-4

How to cite this article:
Mostafa Eissa MEA. Statistical analysis of the critical quality attributes of 1,2-dihydroxypropane as a pharmaceutical excipient. German J Pharm Biomaterials. 2024;3(3):9-17.