DEVELOPMENT OF AUTOMATED METHADONE DISPENSER FOR DRUG ADDICTION THERAPY

MUHAMAD FARHAN MOHD MAZLAN

FACULTY OF ENGINEERING
UNIVERSITI MALAYA
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MUHAMAD FARHAN MOHD MAZLAN

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DEVELOPMENT OF AUTOMATED METHADONE DISPENSER FOR DRUG ADDICTION THERAPY

ABSTRACT

Drug abuse and drug addiction are becoming growing issues in most countries worldwide and are considered major public health problems. An initiative has been introduced in Malaysia via the methadone maintenance treatment program since the year 2005. Although the program has shown gradual success over the years by reducing the relapse rate of the patients, it has encountered several challenges in maintaining the effectiveness of the manual dispensing method done by using syringe. Therefore, an automated methadone dispenser was developed to improve its effectiveness with the usage of peristaltic pumps and load cell sensors as the main dispensing mechanism. In this research, the reliability and feasibility of the dispenser were determined through percentage error, accuracy and repeatability, and efficiency tests, respectively. The experiment started with sugar solution preparation by dissolving 66.6mg of sugar in 50ml of distilled water. The dynamic viscosity of the sugar solution prepared is 36.680 mPa.s compared to 37.286 mPa.s for methadone syrup resulting in percentage error of 1.625%. Sugar solution was dispensed from 2ml to 50ml in increments of 2ml by using methadone dispenser and manual technique. It was found that the Pearson coefficient for methadone dispenser and manual technique is 0.998 and 0.994 respectively. Performance evaluation was carried out by comparing the volume dispensed and time taken to dispense 16 ml of sugar solution using manual technique which is syringe and beaker, and methadone dispenser for 100 runs. Based on the performance evaluation, the findings suggested that the automated methadone dispenser has contributed to the decrease in percentage error from 8.58% to 1.50% and improved dispensing time by 81.69%. The methadone dispenser also increases the dispensing accuracy by 4.0% compared to current manual methadone dispensing practices.

Keywords: Automated dispenser; Performance evaluation; Drug addiction therapy

PEMBANGUNAN MESIN PENDISPENSAN METADON AUTOMATIK UNTUK TERAPI PENAGIHAN DADAH

ABSTRAK

Penyalahgunaan dan penagihan dadah adalah isu yang kian meruncing di kebanyakan negara dan dianggap sebagai masalah kesihatan umum yang utama. Satu inisiatif telah diperkenalkan di Malaysia melalui program rawatan terapi gantian menggunakan metadon sejak tahun 2005. Walaupun program ini telah menunjukkan keberkesanannya dalam mengurangkan kadar berulang dikalangan pesakit, program ini menghadapi beberapa cabaran dalam mengekalkan keberkesanan proses pendispensan manual yang dijalankan oleh pengamal kesihatan yang diiktiraf. Oleh itu, sebuah mesin pendispensan metadon automatik telah dibina bagi meningkatkan kecekapan dan mematuhi tuntutan serta keperluan pengguna dengan menggunakan pam peristalsis dan sensor sel beban sebagai mekanisma pendispensan utama. Dalam penyelidikan ini, kebolehpercayaan dan kebolehlaksanaan mesin ini ditentukan melalui beberapa ujian iaitu peratusan kesilapan, ketepatan dan kebolehulangan, serta ujian kecekapan. Ujikaji dimulakan dengan penyediaan larutan gula dengan melarutkan 66.6mg gula dalam 50ml air suling. Kelikatan dinamik bagi larutan gula yang disediakan adalah 36.680 mPa.s berbanding 37.286 mPa.s bagi sirap metadon yang menghasilkan peratusan ralat 1.625%. Larutan gula didispens dari 2ml kepada 50ml dengan peningkatan 2ml menggunakan pendispensan metadon dan teknik manual. Analisa Pearson bagi pendispensan metadon dan teknik manual masing-masing adalah 0.998 dan 0.994. Penilaian prestasi dijalankan dengan membandingkan isipadu dan masa diperlukan bagi proses pendispensan 16ml larutan gula bagi 100 kali menggunakan teknik manual iaitu picagari dan bikar, dan pendispensan metadon. Berdasarkan penilaian prestasi yang telah dijalankan, penemuan tersebut menunjukkan bahawa mesin pendispensan metadon automatik ini telah menyumbang kepada penurunan peratusan kesilapan daripada 8.58% kepada 1.50% dan penambahbaikan masa pendispensan sebanyak 81.69%. Mesin pendispensan metadon ini juga telah meningkatkan ketepatan proses pendispensan metadon sebanyak 4.0% berbanding dengan amalan pendispensan metadon secara manual yang diamalkan sekarang.

Keywords: Mesin pendispensan automatik, Penilaian prestasi, Terapi penagihan dadah.

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LIST OF SYMBOLS AND ABBREVIATIONS

SDGs	:	Sustainable Development Goals
MMT	:	Methadone Maintenance Treatment
MEs	:	Medication Errors
UoD	:	Universe of Discourse
SQL	:	Structured Query Language
HTTP	:	Hypertext Transfer Protocol
PHP	:	Hypertext Preprocessor
ORMs	:	Object-Relational Mappers
MVC	:	Model View Control
API	:	Application Programming Interface
HTML	:	Hypertext Markup Language
CSS	:	Cascading Style Sheets
MVVM	:	Model-View-View-Model
DOM	:	Document Object Model
UNODC	:	United Nations Office on Drugs and Crime
PWID	:	Person who inject drugs
HIV	:	Human Immunodeficiency Virus
CAD	:	Computer-Aided Design
LED	:	Light-emitting diode
NCAIDS	:	National Centre for AIDS/STD Control and Prevention
China CDC	:	Chinese Centre for Disease Control and Prevention

LIST OF APPENDICES

CHAPTER 1: INTRODUCTION

1.1 Introduction

Substance use such as opioids is a major cause of disability globally which has become one of the major risk factors for the burden of disease worldwide, with 11% of the total health burden (Forouzanfar et al., 2015). This issue has been proved by the United Nations Sustainable Development Goals (SDGs) which is shown by the amount of treatment coverage for substance use disorder throughout the year in 26 countries (Degenhardt et al., 2017). Most of the drug addicts have been using it for years and some of them have experience joining the rehabilitation centre. However, most of them are unable to fully recover due to stigma and perceptions of the community (Luo et al., 2019). Stereotypes and prejudicial attitudes in the community might weaken their willingness to access healthcare (Borders et al., 2015) and adhere to the treatment which might affect their health (Chakrapani et al., 2014; Mburu et al., 2018).

Malaysia, as one of the countries facing the problem, has spent a significant amount of financial resources in an attempt to overcome the drug addiction problem (Kamarulzaman, 2009). Methadone maintenance treatment (MMT) is one of the initiatives introduced in 2005 that has been used to treat opioid dependence (Ali et al., 2016). Methadone is a potent synthetic opioid agonist which can be administered orally, daily to achieve a steady-state plasma level after repeated administration (Lewis, 1997). Although it has almost the same effect as other opioids such as morphine, consuming methadone at a certain therapeutic dose will reduce craving and dependence while preventing the withdrawal effect (Abdel, 2006). Besides, the MMT program has been shown to be a cost-effective alternative which can reduce illicit drug use and crime rate significantly while improving social productivity (K. E. Moore et al., 2018).

However, an increase in drug addicts participating in the MMT program has resulted in more workload on the pharmacists (B. A. Moore et al., 2013). Dispensing methadone continuously by using syringes due to the increased workload exposed pharmacists to the risk of musculoskeletal disorders such as carpal tunnel syndrome (CTS). Besides, the excessive workload may lead to medication errors (MEs) which can cause unintended treatment results or death (Makary & Daniel, 2016). A dispensing error which is a type of MEs can be defined as discrepancies between medications that were prescribed and dispensed (Velo & Minuz, 2009). The manual dispensing method which is widely used has a higher risk of dispensing error due to it being more prone to human error.

Pharmacy automation as means of technological intervention can be very beneficial in carrying out regular, repetitive tasks such as dispensing medicine which does not require complicated decision-making. An automated dispenser has been developed to improve the efficiency, accuracy and dispensing time of the dispensing process. There is an automated methadone dispenser developed to dispense methadone prescriptions according to the volume and dispensing time specified for drug addiction therapy (Amran et al., 2019). Thus, removing the need to dispense and measure the methadone syrup manually for each patient. However, the dispenser can only dispense one prescription at a time which is less efficient for patients who are stable and eligible for take-home doses.

In this thesis, a methadone dispenser for drug addiction therapy equipped with seven outlets is proposed to improve dispensing efficiency, accuracy and repeatability, while reducing dispensing time, dispensing errors and occupational hazards for pharmacists.

1.2 Problem Statement

The main problem in the current research is the reliability of peristaltic pumps and load cell sensors in the automated methadone dispenser as the dispensing mechanism instead of the current manual technique. The new alternative is introduced because the current manual dispensing technique by using syringe and beaker to measure and dispense the methadone syrup is inefficient, has wider range of volume dispensed and prone to human error. Based on the analysis done on the dispensing process by one of the pharmacists, it is found that the volume distribution is wide and inconsistent. Besides, the time taken for the pharmacist to dispense a certain number of prescriptions takes a long time which reduces the efficiency of the whole process. So, it is important to ensure the viability and suitability of the new alternative to prove that the process can be successfully improved.

The pump which dispenses the liquid must function according to the reading obtained by load cell sensor to ensure the accuracy of the liquid dispensed. Thus, performance evaluation must be carried out as it allows analysis to be done. Once the automated methadone dispenser is evaluated, discussed, and justified, then it can be proven to be more efficient and accurate as well as viable to replace the current manual dispensing technique. The performance that will be evaluated can be divided into several parts which are accuracy, repeatability and dispensing time. Then, the performance will be compared with the current manual technique to discuss the difference and improvements made.

Next, the problem in testing the new device is the availability of methadone syrup to be used. Methadone is a controlled drug which can only be prescribed by licensed healthcare professionals to specific individuals. So, the methadone syrup cannot be used in the research to test the newly developed dispenser. To overcome the problem, a methadone syrup substitution is carried out. The substitute is required to have approximate properties such as dynamic viscosity compared to the methadone syrup to ensure that the performance evaluation can be conducted accurately. In this thesis, a sugar solution substitute is prepared to be used for the testing and performance analysis. The dynamic viscosity is considered since the testing involves dispensing process by the peristaltic pump for automated dispenser and syringe for manual technique.

1.3 Research Objectives

The scope of this research is to design and develop an automated methadone dispenser for drug addiction therapy. The objectives are listed as follows:

1. To study and develop an automated methadone dispenser equipped with seven peristaltic pumps and load cell sensors that will assist and enhance the methadone dispensing process in MMT program.
2. To evaluate and analyze the performance of the developed automated methadone dispenser compared to the manual dispensing method in terms of accuracy and repeatability of the volume dispensed, and dispensing time.

1.4 Scope of Research

The research focuses on studying and analyzing the performance of the automated methadone dispenser equipped with seven outlets to be implemented for drug addiction therapy. This study is important to ensure that the alternative proposed for the dispenser to use peristaltic pumps and load cell sensors as dispensing mechanism can provide the methadone syrup according to the requirements with better accuracy, precision and efficiency compared to the current manual dispensing technique. This is because the current manual dispensing technique uses syringes and beakers to dispense the methadone syrup which takes time, is inefficient and has the risk of error. Besides, the seven outlets and tubing system introduced to allow the dispensing of seven bottles simultaneously are more efficient and time-saving for patients who are eligible for take-home dose as up to seven identical prescription.

The research starts with the design and modelling process of the automated methadone dispenser which is then fabricated. After the component selection and development process, the components of the dispenser such as load cell sensors and peristaltic pumps were programmed to ensure the dispensing process can be carried out. Meanwhile, sugar solution substitution is prepared for the performance evaluation by dissolving a specific amount of sucrose into fixed volume of distilled water. The properties of the solution prepared which is the dynamic viscosity is measured by using a viscometer to ensure that the viscosity is equal to methadone syrup viscosity. Once the methadone dispenser is ready, performance evaluation is carried out to analyze its performance in terms of accuracy, repeatability, and dispensing time. This is to ensure that the peristaltic pumps and load cell sensors in the dispenser can replace the syringe usage of the current manual technique while providing improvement to the overall dispensing process of methadone in drug addiction therapy.

Hence, the scope of the research is to study, develop and analyze an automated methadone dispenser equipped with seven outlets and conduct performance evaluation of the automated methadone dispenser compared to the current manual dispensing method in terms of accuracy, repeatability, and dispensing time.

1.5 Summary

Based on the current situation of the drug addiction problem, the increase in the number of patients in drug addiction therapy has increased the workload of pharmacists. Increased workload and continuous dispensing tasks performed by the pharmacists by using syringe and beaker led to performance reduction and a higher risk of dispensing error.

Therefore, usage of automated methadone dispenser equipped with seven outlets consisting of peristaltic pumps and load cell sensors as the dispensing mechanism is studied and proposed to overcome the problem. To ensure the feasibility of the methadone dispenser, performance evaluation and analysis is carried out to compare the performance and reliability between the methadone dispenser using peristaltic pumps and load cell sensors as dispensing mechanism, and manual technique using syringe and beaker in terms of accuracy, repeatability and dispensing time. The analysis is carried out by dispensing a constant volume for a number of runs as well as dispensing a series of volume with an increment to study the accuracy of the peristaltic pumps and load cell sensors.

The research is carried out by designing the methadone dispenser which is followed by a study and research on the suitable components to be assembled and fabricated according to the model made. Based on the study and literature review that have been done, methadone syrup substitution is prepared by dissolving a specific amount of sugar into distilled water. After the circuit and program of the dispenser are done, testing and performance evaluation is carried out to compare the performance with the manual technique. The testing process is carried out by dispensing a fixed amount of liquid using both dispensing techniques which the volume and time taken for each run is recorded.

1.6 Organization of Thesis

This thesis contains five main chapters as described in the outline shown in Figure 1.1.

Chapter 1: Introduction

This chapter describes the introduction of the study. A brief background of the study such as drug addiction therapy will be presented. This chapter will also include the problem statement, research objectives and the scope of the research.

↓

Chapter 2: Literature Review

This chapter consists of a literature review which summarizes past studies done by others, which started with the general idea of an automated dispenser and automated dispenser as a medical device-based application, followed by a database system in web application, methadone maintenance treatment (MMT) program and automated methadone dispenser for MMT program. The chapter also includes a summary which concludes the chapter and states the research gaps identified.

↓

Chapter 3: Research Methodology

This chapter describes the methodology proposed to conduct the study and achieve the objectives. The chapter discusses methadone dispenser design and methadone dispenser development which can be divided into three parts which are mechanical, electrical, and programming and software parts. The chapter also discusses the methodology for the performance evaluation of the methadone dispenser which consists of the preparation of sugar solution as methadone substitution, accuracy and repeatability analysis, and efficiency analysis. Lastly, this chapter discusses database system development.

↓

Chapter 4: Results & Discussions

This chapter describes the results obtained and discussions made based on the results. The results consist of the automated methadone dispenser that has been developed, the sugar solution prepared for the methadone substitution, performance evaluation based on accuracy, repeatability and efficiency, and a database system in a web application that has been developed.

↓

Chapter 5: Conclusions & Recommendations

This chapter summarises and concludes the results and discussions that have been made. This chapter also discusses the limitations of the study when conducting the research and recommendations for future works to further improve the current research.

Figure 1.1 Thesis outline

CHAPTER 2: LITERATURE REVIEW

2.1 Automated Dispenser

The automated dispenser has been used in many sectors due to the improvement mainly in terms of efficiency that it offered. As an example, a liquid dispenser used in the colour industry is designed and fabricated (Khatod & Sakhale, 2012). The main objective of the research is to overcome the disadvantages of the current manual technique which are costly, complex, and hard to operate. Besides, the research also aimed to improve the accuracy of the dispenser. Liquid dispensers can be divided into four types according to the basis of application as shown in Figure 2.1 (Khatod & Sakhale, 2012).

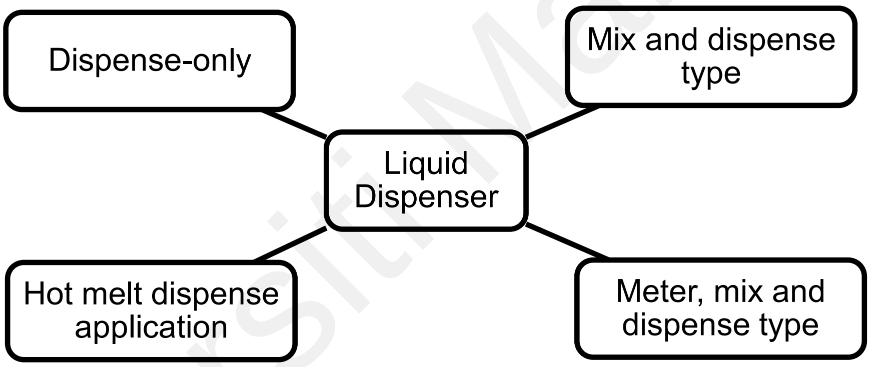

Figure 2.1 Types of liquid dispensers (Khatod & Sakhale, 2012)

The automated liquid dispenser has been applied in the food & beverages industry. This is because a dispenser is a practical and useful technique of dispensing a certain, preset amount of product through a production system ('Improving Batch Dispensing in the Food and Beverage Industry', 2018). The new technique reduces product handling which decreases batch production time and increases consistency and efficiency among batches. An automated bar dispenser is developed to measure the pour sizes and record them in the database (Istocka, 2015). This method allows record comparison with the sales database to track losses. Since the customers can use the dispenser themselves, the system expanded to self-served customers without the need for a bartender.

2.1.1 Automated Dispenser as Medical Device-Based Application

Automated dispensers are a convenient alternative for patients to receive drugs with the condition that the pharmacists can intervene when needed before the administration of drugs. Recently, automation technology and intervention have been implemented in the medical field (Bajaj, 2018) as healthcare institutions such as hospitals and clinics have been searching for enhancements and innovative solutions for better patient safety quality (Tsao et al., 2014). The current technology and advancements have enabled rapid growth and development in medical device innovations (Hoadley & Ananthan, 2013), specifically in the pharmacy department (Chapuis et al., 2015). This might be due to the requirement for the medication dispensing process at every level to be more efficient and safer with a low risk of medication errors (MEs) (van den Bemt & Egberts, 2007). MEs are likely to happen due to the nature of the human itself causing an error (Rabiu et al., 2014). Besides, the dispensing process by using manual techniques such as using a spatula, simple tray, beaker, and syringe is time-consuming (Embrey, 2012).

Hence, MEs have to be controlled and avoided due to the threat of causing drug-related complications to the patients (Meyboom et al., 2000). The factors that cause MEs were discussed and clarified by Amran et al. (2019) where they happened due to the lack of skills and knowledge, distraction on the pharmacists, and high pharmacists' workload. A higher risk of MEs can also be caused by the working environment itself (Salmasi et al., 2015). Figure 2.2 shows the types of MEs that normally occur in pharmaceutical patient care (Cheung et al., 2009) and the most common errors in dispensing errors include dose omission (Anselmi et al., 2007), wrong dose (Teagarden et al., 2005), and wrong dispensing time (Barker et al., 2002). The problem is becoming more serious over the years due to the increased workload among healthcare professionals caused by the increase in prescription demand (Li & Yoon, 2015). In this thesis, the research aimed to address one of the dispensing errors which is wrong dosage or medicine quantity. This is a dangerous error as it can cause serious effect such as overdose to the patient when inaccurate dose is administered or consumed.

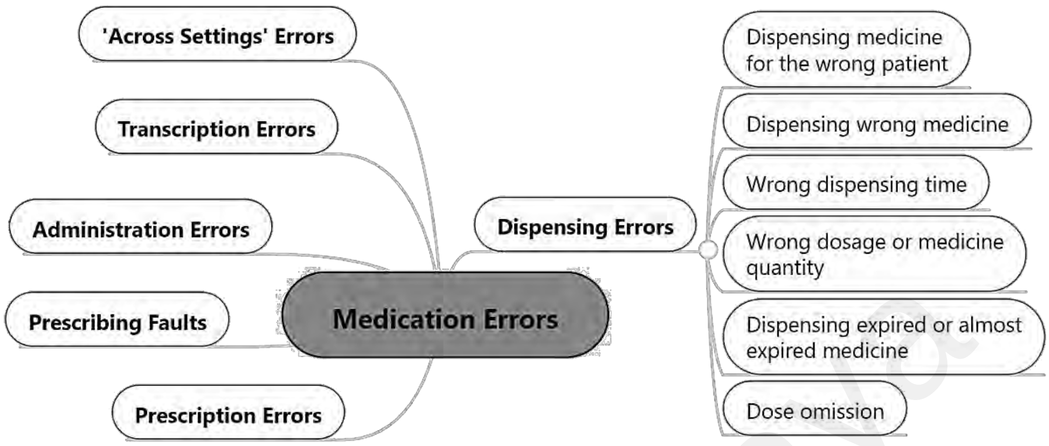

Figure 2.2 Type of medication errors (Ashcroft et al., 2005; Beso et al., 2005; Chua et al., 2003)

Hence, implementation and usage of an automated dispenser have been introduced in the medical field such as pharmacy departments with the main objective to reduce those errors (Darwesh et al., 2017) and reducing direct human involvement in the dispensing and prescription process (Aldossary, 2016). Besides, the implementation of automated dispensers contributed to patient outcomes improvement (Chapuis et al., 2010). Other advantages of automated dispensers consist of improved productivity (Liu & Fu, 2020), time reduction caused by movement removal and routing speeds enhancement (Amran et al., 2018), removal of expired drugs possibility (Hachemi & Rabhi, 2014), and create a safer and more efficient prescription retrieval (Martin et al., 2000). Besides, automated dispenser introduction lowers the overall cost of healthcare services required for patient care (Nabelsi & Gagnon, 2017).

The development of automated dispensers becomes more compact and simplified throughout the years due to the advancement of technologies. As an example, the biggest difference between the automated dispenser developed in the early 1990s and the more recent dispenser is the size. The dispenser reported by Ishizuka et al. (1991) as shown in

Figure 2.3 (a) is bigger and bulkier compared to the more recent dispenser discussed by Ahadani et al. (2012) and Penna et al. (2017) as shown in Figure 2.3 (b) and (c) respectively.

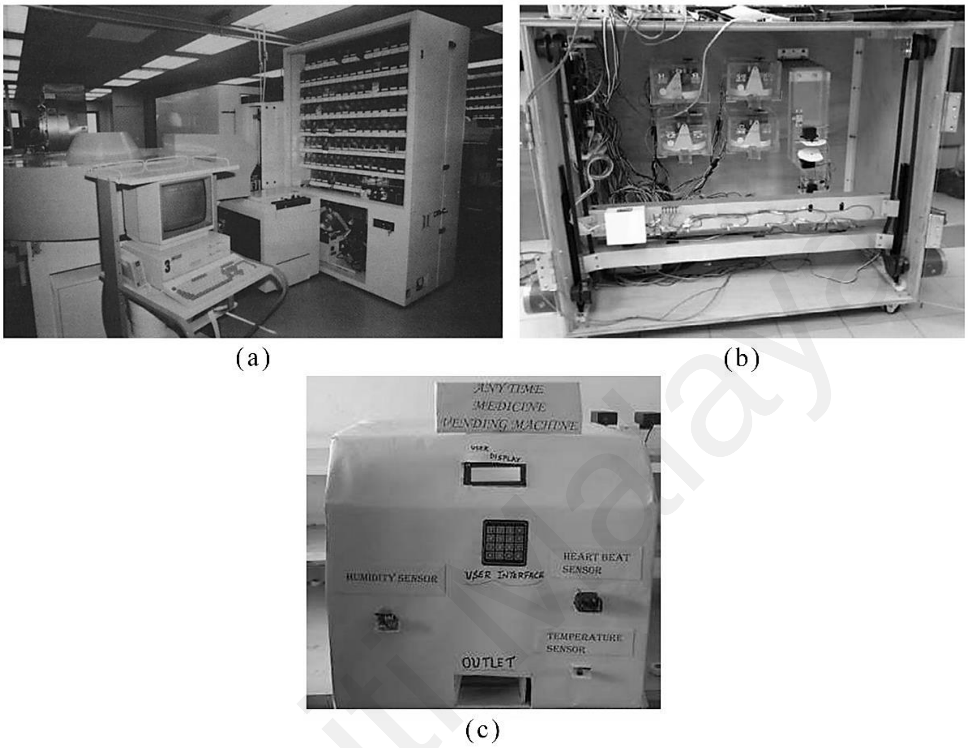

Figure 2.3 ADMs developed by (a) Ishizuka et al. (1991), (b) Ahadani et al. (2012) and (c) Penna et al. (2017)

A low-cost moveable hands-free robotic medicine dispenser that can store up to four different types of pills was developed as shown in Figure 2.3 (b) (Ahadani et al., 2012). The dispenser prototype was developed by using cheap and easy-to-acquire materials. The usage of a simple pulley and belting system ensured a hands-free dispensing process. The inner cell was made from disposable material to ensure the device's hygiene. The addition of wheels allows the device to be moved easily. However, a limited number of pills can be stored at one time due to the size of the storage to maintain its low-cost aspect.

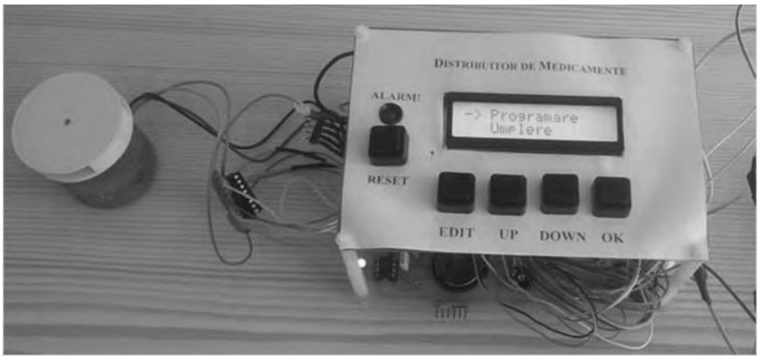

Figure 2.4 Pill dispenser with circular container (Fărcaş et al., 2015)

Another automated dispenser that can dispense medicine into a smaller compartment at a specified time based on the doctor's prescriptions was developed as shown in Figure 2.4 (Fărcaş et al., 2015). Then, the user will be notified by a beep sound. The dispenser was designed with an opening at the top and bottom part of the containers for filling and dispensing respectively. The usage of the PIC18F458 microcontroller allows the dispenser to be programmed for four-time periods of dispensing process daily. Thus, ensuring flexibility to adjust the dispensing time according to a specific patient's prescriptions. The design of the dispenser also makes it suitable for hospital and personal use.

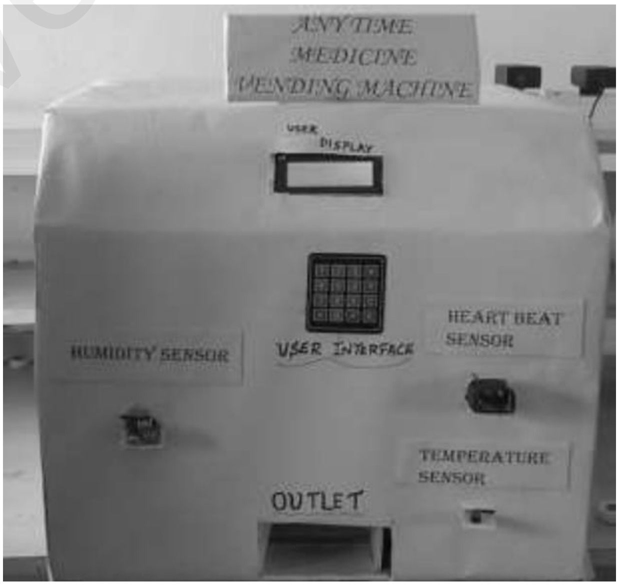

Figure 2.5 Automatic medicine dispensing machine for common sickness (Penna et al., 2017)

A dispenser that can provide basic medicine for common sicknesses such as fever and headache is developed (Penna et al., 2017). The usage of different sensors to check the heartbeat and temperature of the user allows the dispenser to evaluate the user's condition and provide suitable medication. The dispenser was placed in a rural area due to the limited healthcare access in the area and to remove the need for the patient to go to an urban area to obtain basic medicine.

To improve the efficiency of the prescription dispensing process, a dispenser dispenses medicines based on the prescriptions given by the doctor in the form of individual distinct barcodes (Suganya et al., 2019). The dispenser is integrated with a cloud system to store the registered patients' information. Thus, the patient who received the barcode from the doctor can go to any pharmacy using the database to get their prescriptions. This method ensures correct prescriptions and reduces the risk of wrong medicine and dosage.

There is also a simple and easy-to-handle dispenser that consists of multiple slots to store different types of pills (Ramkumar et al., 2020). The dispenser receives the prescriptions from the doctor and stores them in the cloud. After accessing the patient's details, the medicines are dispensed, and the record is updated. The simple dispensing steps make the device suitable for the elderly.

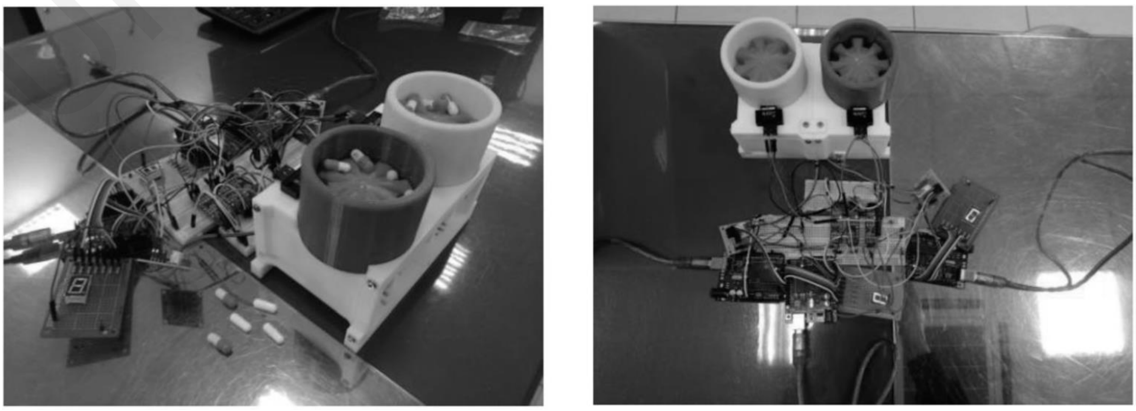

Figure 2.6 Automated medicine dispenser with convolutional neural network image recognition and 3D printing technology (Tsai et al., 2020)

A medicine dispenser for personal use is developed which uses convolutional neural network image recognition to identify the type of pills stored (Tsai et al., 2020). Most of the parts for the dispenser prototype were fabricated by using the 3D printing technique. The user can set the medication type and consumption time remotely by using a smartphone that has been connected to the dispenser. Besides, the dispenser will remind the user to take the prescriptions set through the smartphone.

The implementation of an automated dispenser is not only to decrease the MEs but to ensure the adherence rate as it is one of the major problems encountered by healthcare institutions (Santra, 2015; Sarna et al., 2008). Medicine adherence among the elderly was a major issue (Mukund & Srinath, 2012). For instance, the elderly with Parkinson's disease have an increased risk of them failing to consume the medication at the specified time which worsens their condition (Palmer, 2020). Moreover, problems such as mobility problems (Kulkarni et al., 2008), problems in remembering the medication time (Eippert, 2008) and ignorance of medicine consumption instructions have also caused medication non-adherence. These problems are accountable for approximately 8-11% of hospital admission for elderly patients (Vik et al., 2004), and 20% of the patients fully forget their prescribed medications (Elliott, 2006). In general, the non-adherence to prescribed medication was clinically significant in 55.1% and 69.6% of the patients at the first and second follow-ups respectively (Pasina et al., 2014). Hence, the implementation of an automated dispenser will not only guarantee medication adherence, but the medicines stored by the automated dispenser allowed accurate medication usage, and both tracking and recording of staff access (Roman et al., 2016).

Research variables are important to ensure the analysis carried out on the study is aligned with the research objectives. In research done by Srinivasan et al. (2018), the accuracy of the device is analysed by measuring each dispensing volume from 1ml to 5ml in increments of 0.5ml. In their research, a precision medication dispenser is proposed for pediatric patients. For comparison in accuracy, they also dispensed the liquid medication with a standard oral syringe supplied with the oral medication (Srinivasan et al., 2018).

In another research, a liquid medication dispensing robot is studied and evaluated by dispensing 18 different liquid medications in a medicine cups using an automatic in-line checkweigher (Lagrange & Lagrange, 2023). The accuracy, repeatability and intermediate precision are analysed based on the data obtained. In another research, measuring device for liquid dispensing is studied and developed (Shumate et al., 2018). The performance of the device is studied by running a pilot test where the results from the device are compared with traditional method of quality control in which the operator manually carried out the weighing process.

2.2 Methadone Maintenance Treatment (MMT) Program

Drug addiction has been viewed as a chronic disease that needs long-term treatment, therapy and support (Chen et al., 2017). Opioids continue to be responsible for the largest burden of disease related to drug use (*UNODC World Drug Report 2021*, 2021). MMT has been used to treat opioid addiction in many countries since the 1950s ('Methadone Maintenance Treatment', 2009). Methadone is a long-acting synthetic opioid that is initially developed for pain control and is now primarily used for the therapy of opioid addiction (Corkery et al., 2004). The MMT program aims to reduce addiction and craving for opioids among the person who inject drugs (PWID) (Hoadley & Ananthan, 2013). The opioid-dependent patient consumes a dose of methadone syrup orally which leads to a reduction of cravings for opioids and withdrawal symptoms.

Although methadone is addictive like other opioids, being on methadone is not the same as being dependent on illegal opioids such as heroin. This is because it is safer for the patient to consume methadone under medical supervision than it is to take heroin of unknown concentration. Besides, methadone is taken orally, unlike heroin which is often injected and can lead to HIV transmission if needles are shared. MMT also reduces the number of deaths from a drug overdose in prisons (Hedrich et al., 2012), which is the leading direct cause of death over a fortnight following the release from prison (Merrall et al., 2010). Besides, the MMT program improves the quality of life and reduces criminal behaviour and mortality rate (Frimpong et al., 2017).

In the year 2005, Malaysia initiated the MMT program as Malaysia was in the throes of one of Southeast Asia's most explosive epidemics of HIV infection (Wickersham et al., 2013). The epidemic was largely concentrated among PWID, especially opioids, who consist of more than 1.3% of the population ranging from 15-64 years. Wickersham et al. (2013) also reported that half of the new HIV infections among PWID in Malaysia are related to opioids. Since the implementation of the MMT in Malaysia, the frequency of HIV infection among drug users has been reduced from 74.7% in the year 2000 to approximately 5% by the year 2019 (*GLOBAL AIDS MONITORING 2020: Malaysia HIV/AIDS Progress Report*, 2020).

Other than Malaysia, countries including China and Vietnam have also been implementing MMT programs to overcome opioid dependence. Other nations including Canada, Australia and the United Kingdom have introduced and conducted the MMT program where the PWID are allowed to receive therapy and prescriptions from community treatment centres (Kleinman, 2020). China has expanded the MMT program rapidly (Yin et al., 2010) after the initial accomplishment of small-scale pilot MMT programs implemented in the year 2004 (Pang et al., 2007). Wuhan, which is a sprawling and populated city in main China with a population of approximately 10 million has 20 clinics offering MMT services with a cumulative enrolment of over 16,000 patients from the year 2006 to the year 2010 (Marienfeld et al., 2015).

In the MMT program, the first dosage of methadone syrup prescribed to the patient is low which is normally ranging from 10-30mg (‘Methadone Maintenance Treatment’, 2009). Then, the amount of the methadone syrup dosage will be progressively increased until the maintenance dose is achieved. The maintenance dosage is the volume of methadone syrup prescription that the patient needs to control the addiction and inhibit opioid withdrawal symptoms but does not cause euphoria. Thus, the clinical practice provides individualized treatment as the methadone dose is regularly customized based on the patient’s particular conditions. The summary of determining the optimal MMT dose for each patient is shown in Figure 2.7. Since the year 2016, Malaysia has allowed the assigned doctors to prescribe take-home doses for patients under certain circumstances for up to six days. The patients are only eligible for the take-home doses after they have been stable for at least six weeks in the MMT program (*Pendispensan Rawatan Terapi Gantian Methadone*, 2017). Besides, evaluations of the patient’s conditions need to be made to ensure that they are eligible for take-home doses.

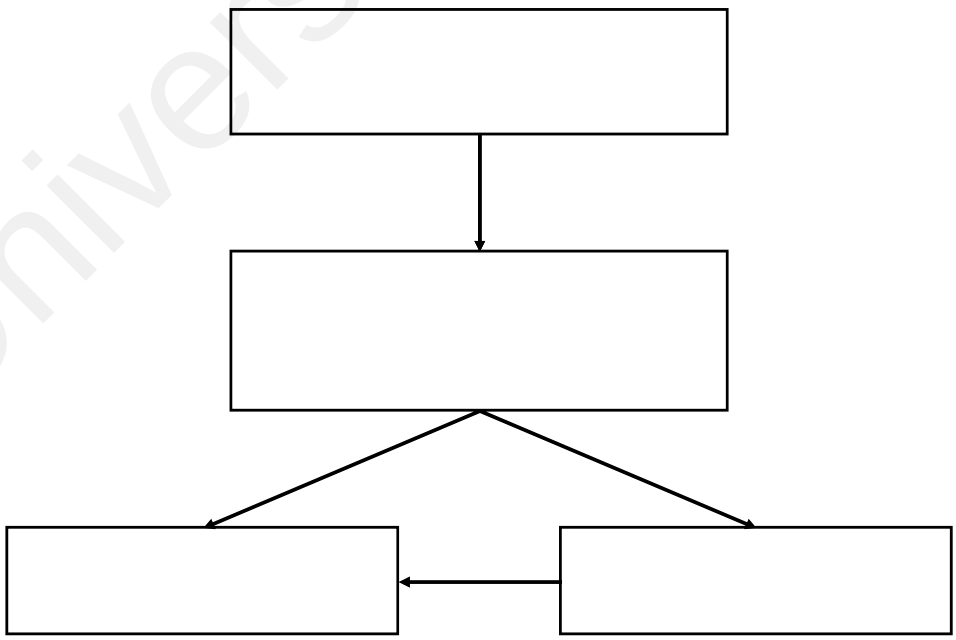

Figure 2.7 MMT dosing flowchart (‘Methadone Maintenance Treatment’, 2009)

Even though the effective dosage of methadone syrup differs for each patient, the common dosage recommended by the clinical standards ranges between 60-100mg/day (Torrens et al., 2015). Research has shown that patients taking methadone doses greater than 60mg daily were less likely to be involved with other opioids and reduce their dependency ('Methadone Maintenance Treatment', 2009). Besides, it is found that the common dosage of methadone prescribed in pharmacies is between 60-80mg (D'Aunno et al., 2019). Alternatively, Wickersham et al. (2013) stated that a dose of 80mg or slightly more had better treatment retention. There is also research that reported average doses ranging from 80 to 100mg/day to have higher rates of patient retention in therapy (Kleber, 2008). There are different opinions from the literature review due to the methadone dosage being determined specifically for each patient as a result of the differences in preferences, individual, circumstances and metabolism (D'Aunno et al., 2019).

2.2.1 Manual Dispensing Technique for MMT Program

Patients in MMT program must receive their dose daily. The methadone dosing prescribed to the patient is strictly managed to minimize diversion which refers to patients giving or selling their methadone syrup to others ('Methadone Maintenance Treatment', 2009). Thus, a well-managed program can reduce the risk of diversion through the introduction of clear dosing procedures. The dosing process should be conducted by nurses or other health professionals under the supervision of nurses. After patient identification and assessment by the nurse, the same nurse must be in charge of the dosing process.

2.2.2 Automated Methadone Dispenser for MMT Program

Most tablets and syrup prescriptions dispensed by pharmacists are done by using a spatula, simple tray, beaker and syringe (Amran et al., 2019). This manual dispensing method is also used for dispensing methadone syrup for the MMT program. Syringes are used to measure the required dose before it is prescribed to the patient. Nowadays, an increase in patients in the MMT program has caused a higher workload for the pharmacist. The dramatic surge in addiction has led to treatment needs that exceed the current methadone treatment system (B. A. Moore et al., 2013). This has reduced the efficiency of the methadone syrup dispensing process and increased the risk of errors in dispensing process. Thus, therapeutic interventions must be introduced to improve the current manual dispensing technique which is susceptible to human error. The introduction and implementation of an automated methadone dispenser is an innovative approach that improves the efficiency and workflow of the pharmacist (Amran et al., 2019). Besides, it reduces the risk of the occupational hazard of musculoskeletal disorders such as carpal tunnel syndrome among pharmacists and minimizes the risk of dispensing errors.

Another automated methadone dispenser prototype has been developed that allows the user to set the dispensing time (Amran et al., 2019). The performance of the prototype was evaluated by dispensing a fixed amount of methadone syrup for several runs. 104mg of methadone which is the standard methadone syrup dosage frequently used in clinical routine was dispensed and repeated for 100 runs. The novelty introduced by the prototype is the ability to control the dispensing time by allowing the user to set the dispensing time during data input. Based on the dispensing time set, the device will configure the flow rate to achieve the required volume during the allocated time.

Figure 2.8 Automated methadone dispenser (Amran et al., 2019)

Although the machine can dispense automatically, it can only dispense one bottle in one run. Thus, an improvement can be done by developing an automated methadone dispenser equipped with seven outlets suitable for patients who are eligible for take-home doses to save time while improving the efficiency of the MMT program.

2.3 Summary & Research Gap

Based on the literature review, many automated dispensers have been developed and implemented in the medical field. The objectives are to improve the workflow of the healthcare professional, improve the efficiency of the prescription dispensing process and reduce the risk of dispensing errors. However, the majority of the dispensers were developed to dispense solid-type medicine such as pills and tablets. Less liquid-type automated dispensers are being reported. From the review, there is only one research found related to the automated dispenser for the MMT program. Furthermore, the dispensers are only equipped with a single dispensing system with one inlet and outlet, making the dispensing process for several prescriptions needed to be done repeatedly which is less efficient, takes more time and has the risk of dispensing errors. Thus, to improve the overall efficiency of the MMT program and reduce the risk of error, an automated methadone dispenser equipped with peristaltic pumps and load cell sensors as dispensing mechanism is proposed. Based on the literature review, the performance of the proposed solution is studied and analysed by dispensing a range of volume in increments and compared with the current method which is by using syringe and beaker. Besides, the device is also evaluated by the performance to dispense different types of liquid.

CHAPTER 3: RESEARCH METHODOLOGY

3.1 Introduction

The current research aims to study and develop an automated methadone dispenser equipped with seven peristaltic pumps and load cell sensors that will assist and enhance the methadone dispensing process in MMT program, and evaluate and analyse the performance of the developed automated methadone dispenser compared to the manual dispensing method in terms of accuracy and repeatability of the volume dispensed, and dispensing time. Based on the current guidelines by Ministry of Health, Malaysia, up to 6 take home doses with approval of methadone treatment team are allowed to be prescribe to the patients (Yuswan & Dazali, 2016). Thus, seven prescriptions are required to be dispensed simultaneously.

The flow of the research for this project can be simplified as shown in Figure 3.1. The flowchart can be further divided into several main tasks as shown in Appendix A. The research started by conducting literature reviews to study the previous research and identify the research gap in the field. Based on the literature review and research gap, the objectives and concepts for the automated dispenser are made. Component selection and dispenser fabrication will be carried out once the model made is finalized. The performance evaluation of the methadone dispenser is conducted after the testing and calibration process to allow data tabulation and discussion to be made.

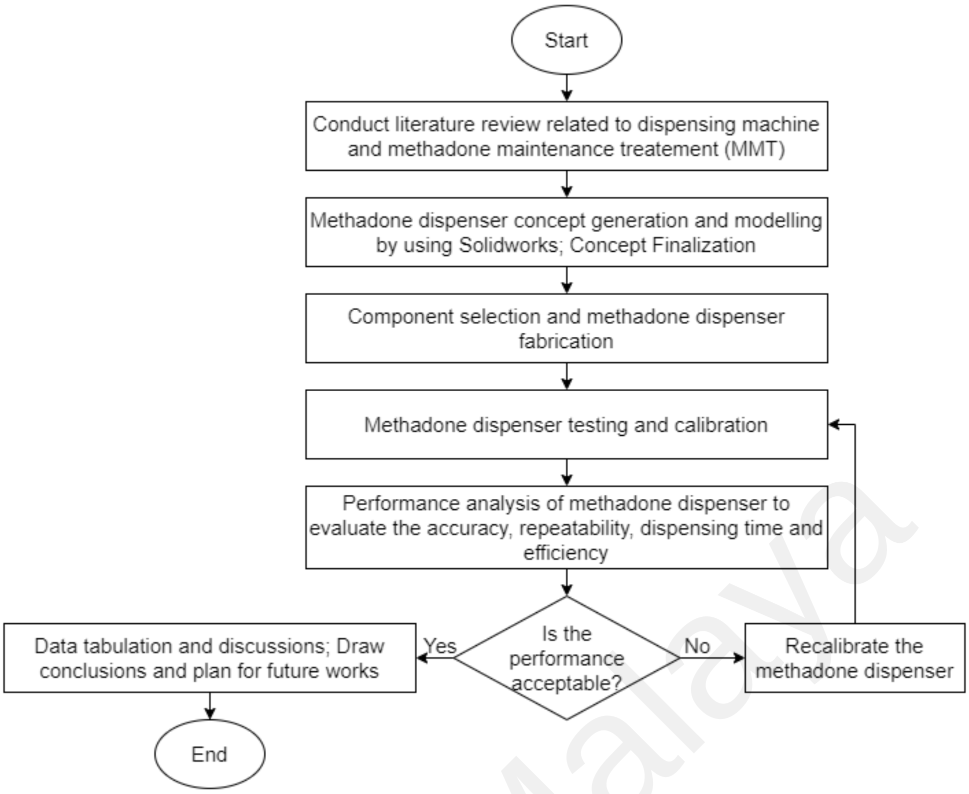

Figure 3.1 Simplified Research Flowchart

3.2 Methadone Dispenser Design

A model made by using CAD software allows an analysis to be carried out to evaluate the viability and machinability of the design. Figure 3.2 shows the detailed flowchart of the concept generation and modelling by using Solidworks. The models of each component for the methadone dispenser are designed and assembled to ensure that there is no interference and that the clearance is acceptable. The models are revised if there is interference present. Once the design for each component has been finalized, the component selection process is carried out.

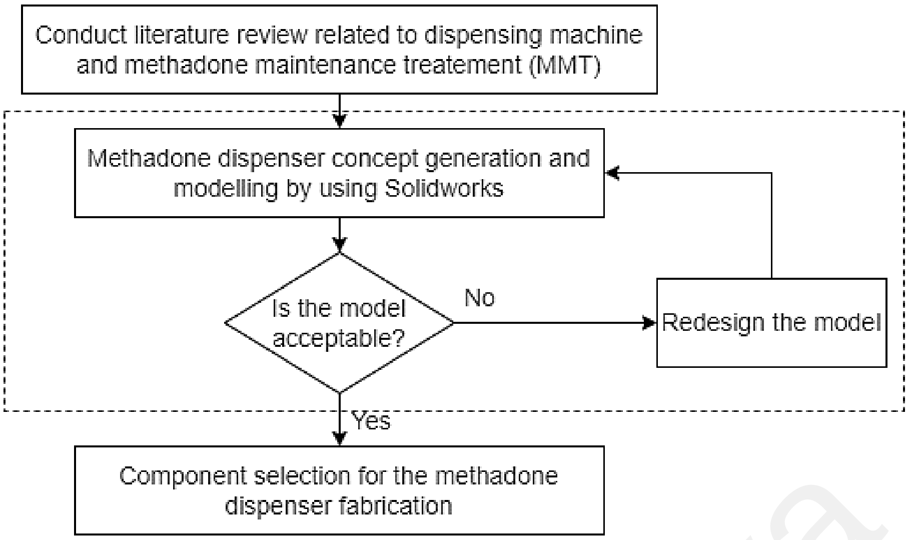

Figure 3.2 Detailed flowchart of methadone dispenser concept generation and modelling by using Solidworks

The modelling of the automated methadone dispenser is carried out by using Solidworks software to visualize the concept. The model for the main housing of the automated methadone dispenser is shown in Figure 3.3. In the figure, the housing of the methadone dispenser comprises several parts such as the main housing, back cover, storage cover, pump cover and bottom cover. The model made allows the components needed to be identified and ensures that the machine can be fabricated. The multiview and isometric view of the assembly, main housing, back cover, storage cover, pump cover and bottom cover are shown in Appendix B, Appendix C, Appendix D, Appendix E, Appendix F, and Appendix G respectively. The drawing includes the general dimensions of the assembly and parts in mm.

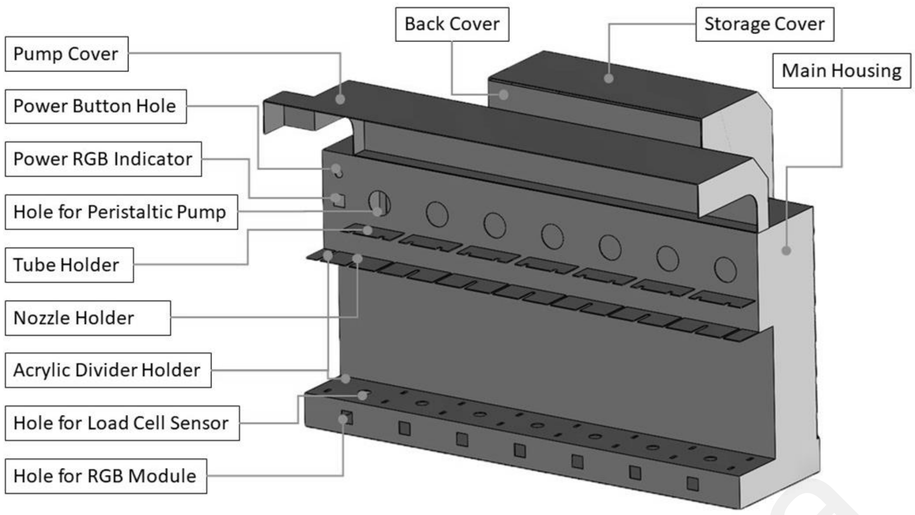

Figure 3.3 Model of the main housing of the automated methadone dispenser

Figure 3.4 shows the bottle base CAD design which is connected to the load cell sensor and used to hold the prescription bottle during the dispensing process. The bottle base is designed according to the prescription bottles that are commonly used by pharmacists to prescribe methadone syrup to patients. Two holes are made to allow it to be connected to the load cell sensor by using screws and nuts.

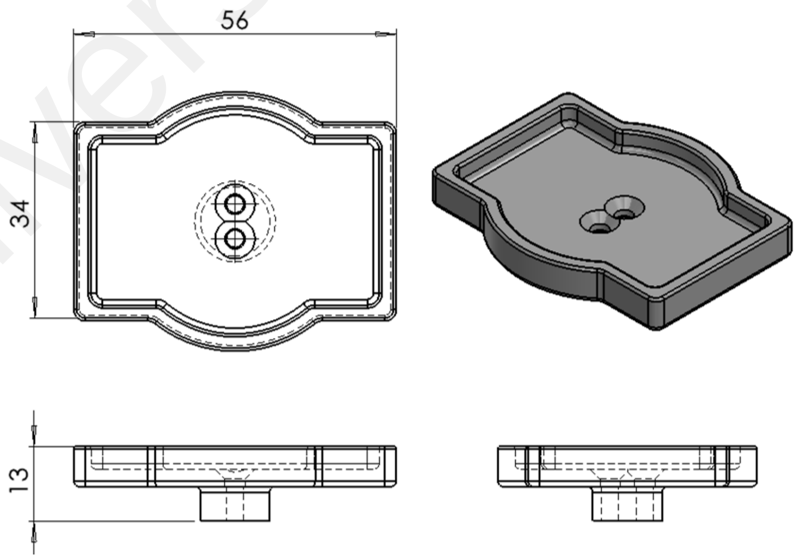

Figure 3.4 Bottle base CAD design

3.3 Methadone Dispenser Development

After the methadone dispenser design is made, component selection and fabrication are carried out. Figure 3.5 shows the detailed flowchart of component selection and machine fabrication. Components selected for the dispenser fabrication can be divided into three parts which are mechanical, electrical, and software and programming. Custom parts such as the dispenser housing and bottle base are designed by using Solidworks. The dispenser is then fabricated, prepared, and calibrated to proceed with the performance analysis to evaluate the functionality of the device.

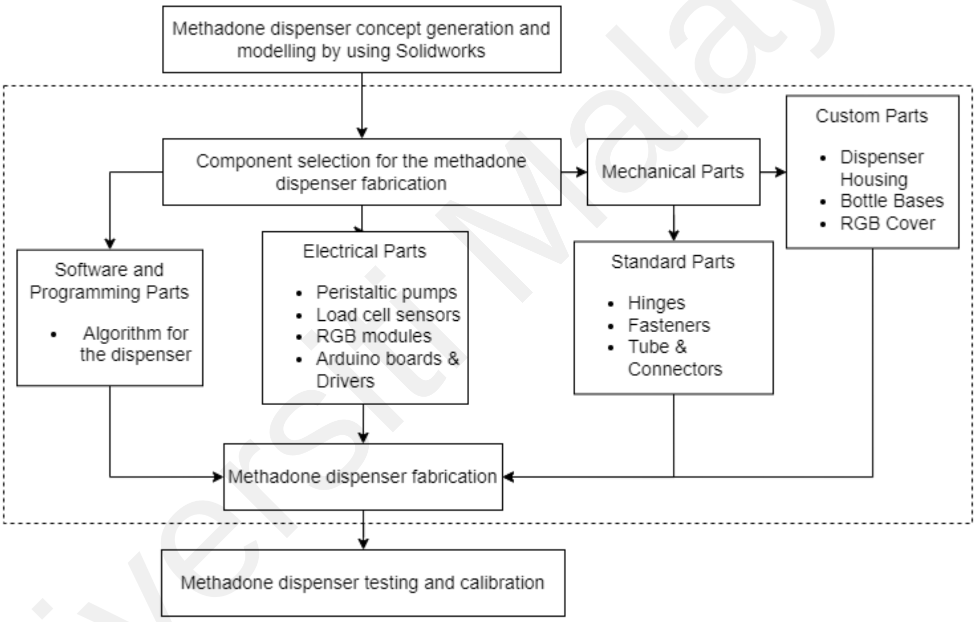

Figure 3.5 Detailed flowchart of component selection and machine fabrication

3.3.1 Mechanical Parts

Mechanical parts of the dispenser consist of the fabrication of the housing such as base, tank casing, top cover and control box which allow additional components such as pumps and sensors to be attached. Seven Grothen GAB26 peristaltic pumps are placed at the outlets as the dispensing mechanism. The pumps are used to dispense methadone syrup at each outlet according to the required volume. The motion of the pumps is controlled by the microcontroller based on the data received by the load cell at each outlet.

Initially, a diaphragm pump and peristaltic pump are considered for the dispenser. Diaphragm pumps and peristaltic pumps are types of positive displacement pumps in which a fixed volume of liquid is forced from the suction or inlet to the discharge chamber or outlet by trapping the liquid into a case (Longo et al., 2017). These types of pumps are considered because the liquid is separated from the energy-imposing parts, unlike other pumps such as dynamic pumps which have direct contact between the liquid and actuation parts such as impellers for the pumping mechanism that might cause contamination. Since the dispenser is used to dispense methadone syrup which is a controlled drug to be consumed, the methadone syrup is ensured to be only making contact with the tube which is food grade. However, the peristaltic pump is chosen as it is more suitable to be used to dispense methadone syrup which is a thick liquid (Korey, 2019). Besides, a peristaltic pump is easier to be used and maintained compared to a diaphragm pump. Furthermore, the peristaltic pump is reversible which suits the function of the dispenser. Peristaltic pumps also allow a high level of sterility as the liquid is only in contact with the flexible tube (Longo et al., 2017).

Connecting the peristaltic pumps to the methadone storage tank and nozzles is 6mm OD food grade silicone tube. Since the length of the tubes differs from each nozzle, the branch length is shown in Table 3.1. The pressure drop for each nozzle can be calculated by using the Hagen–Poiseuille equation as shown in Equation (1)

Table 3.1 Nozzle tube length

Nozzle (Left to Right)	1	2	3	4	5	6	7
Length (m)	0.33	0.25	0.20	0.15	0.20	0.25	0.33

$$\Delta p = \frac{8\mu LQ}{\pi R^4} \qquad \text{Equation (1)}$$

where Δp = Pressure difference between two ends

μ = Dynamic viscosity

L = Length of pipe

Q = Volumetric flow rate

R = Radius

Based on the pump specifications, the motor rotates 180rpm and the flow rate produced by the pump is $3.762\times 10^{-7}\mathrm{m}^3/\mathrm{s}$. The dynamic viscosity of the sugar solution prepared is 36.680 mPa.s. Thus, the pressure difference for each nozzle is shown in Table 3.2. The slight difference in the pressure drop might cause slight inconsistency of the dispensing process. However, the dispensing process is still managed to be completed with small deviations and importantly faster than the manual technique.

Table 3.2 Temperature difference for each nozzle

Nozzle (Left to Right)	1	2	3	4	5	6	7
Length (m)	0.33	0.25	0.20	0.15	0.20	0.25	0.33
Pressure Difference (Pa)	45.296	34.315	27.452	20.589	27.452	34.315	45.296

3.3.2 Electrical Parts

QL-56 load cell sensors were used to control the volume of methadone syrup dispensed by measuring the weight of the methadone dispensed. All the components including peristaltic pumps and load cells were connected to an electrical source and microcontroller to be configured. Thus, the peristaltic pumps will not only dispense the methadone syrup but will also control the amount based on the readings obtained by the load cell sensors and input from the user. When the amount returned by the load cells is equal to the amount inserted by the user, the microcontroller will send a signal to the respective pumps to stop the dispensing process.

The load cell sensor located below the customized bottle base is able to measure the amount of methadone syrup that has been dispensed. Based on the amount of methadone syrup needed that is specified by the user in millilitres, the dispenser calculates and determines the mass required based on the liquid properties which are the concentration and density of the methadone. The calibration process of the load cell sensors is carried out by placing a known and predetermined load onto the load cell sensors in order to check the reading of the mass that the sensors measured. The accuracy and sensitivity of the load cell sensors are configured based on the calibration factor implemented in the algorithm of the methadone dispenser. The calibration and maintenance process of the automated methadone dispenser can be carried out monthly or twice a year based on the requirements.

3.3.3 Programming or Software Parts

The programming part of the machine includes the algorithm made to enable the functionality of the dispenser based on the input inserted such as the volume of methadone syrup prescription and the number of prescriptions bottles required. The program is developed based on the general operational flow of the automated methadone dispensing process as shown in Figure 3.6.

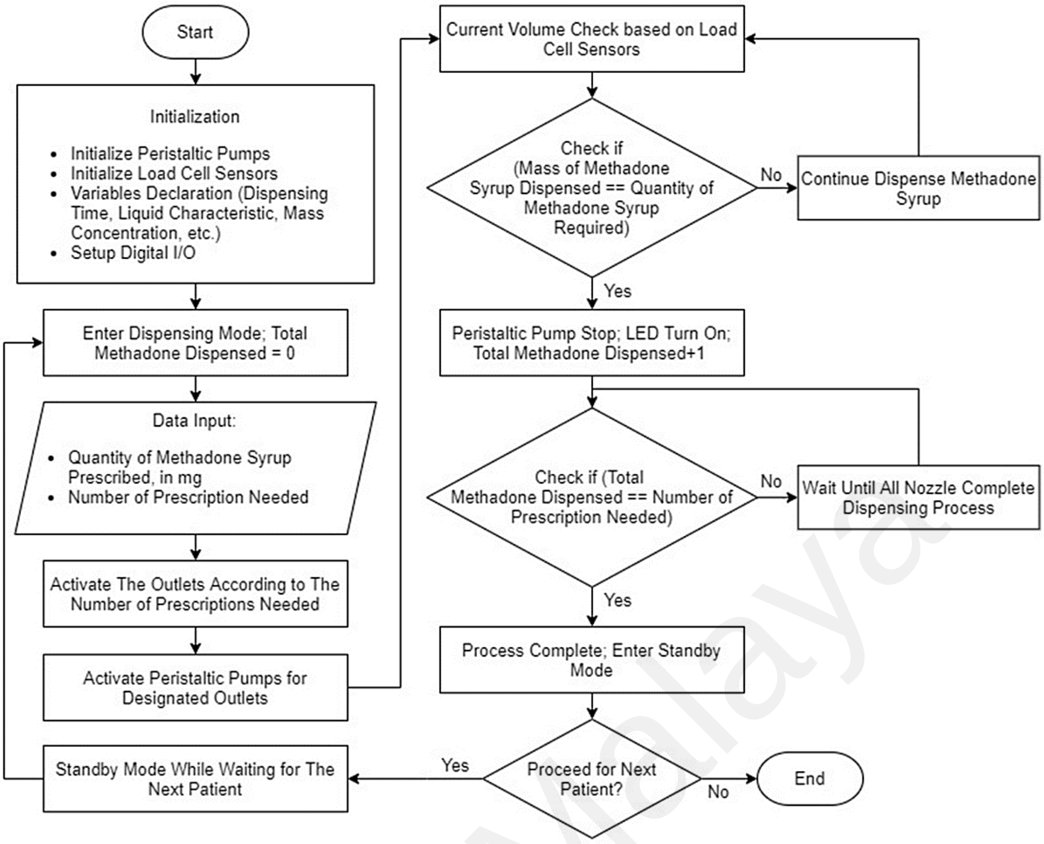

Figure 3.6 General operational flow of the automated methadone dispensing process

The methadone dispenser process begins with the initialization of all parts and components including load cell sensors, motor drivers, RGB module and peristaltic pumps. The parameters of the liquid that will be used during the dispensing process which are liquid density and concentration are also declared. The dispenser then initiates the dispensing mode and set the parameter for total methadone dispensed that functions as the counter for the number of methadone syrup dispensed to zero. Then, the user who is the healthcare professional or pharmacist can insert the amount of methadone syrup needed that is based on the prescriptions of the patient and the number of prescription bottles required by the patient manually to the methadone dispenser. The details such as the methadone syrup amount and the number of bottles are based on the specific patient's prescription records given by the assigned doctor before receiving the prescriptions.

The methadone dispensing process starts by activating peristaltic pumps based on the number of prescription bottles required by the user. The LED that acts as an indicator at each outlet located below the outlet will be powered on once the process at that specific outlet is completed. Once the methadone has been dispensed completely at all respective outlets, the methadone dispenser enters standby mode to allow the user to choose either to continue with the next patient or return to the main menu. Since the methadone dispenser is configured so that one dispensing process is for a specific patient, the amount of methadone syrup dispensed by all outlets is identical in a single dispensing cycle which is based on the amount inserted by the pharmacist prior to the dispensing process. This feature to dispense seven equal amounts of methadone syrup suits patients who are already stable and eligible to take up to six take-home prescriptions based on the doctor's decision.

Next, a program which is a regular user interface and acts as a command window in a device such as a computer or a laptop is developed for user ease. The user interface of the methadone dispenser which allows the user to control the dispenser is shown in Figure 3.7. The interface enables the pharmacist to link with the dispenser to carry out either of the three functions which are Dispense, Flush or Withdraw. To dispense the methadone syrup, the user needs to insert the number of prescription bottles and the quantity of methadone required in either mg or ml. The withdraw function which can be done after the dispensing process is complete will activate the pump at the maximum speed in the opposite direction to suck and send back the methadone syrup left along the tube into the storage tank. This function will avoid the methadone syrup that remained in the tube from being wasted. After the dispensing process is done, the tube can be cleaned by using the flush function. After switching the tank and placing the inlet into distilled water, the flushing process will activate all peristaltic pumps in dispensing direction to dispense the distilled water to all outlets at high speed. The withdraw and flush process will be carried out based on the time specified by the user.

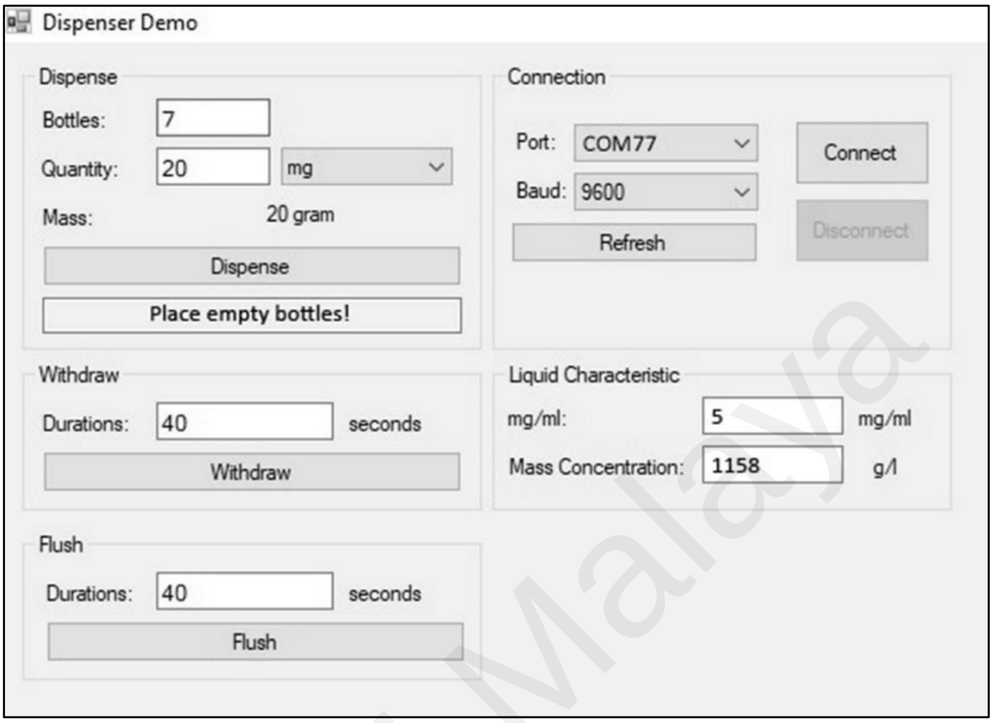

Figure 3.7 User interface for methadone dispenser

Before the dispensing process, the user must declare the liquid characteristics such as the mass concentration (g/l) or density of the liquid and concentration (mg/ml) to suit the methadone batch used. Once the preliminary analysis on the microcontroller is carried out, the baud rate is fixed at 9,600 to can ensure that all the electrical components connected to the microcontroller can function accordingly and properly.

3.4 Performance Evaluation of Methadone Dispenser

Once the methadone dispenser testing and calibration are done, performance analysis can be carried out. Figure 3.8 shows the detailed flowchart of the methadone dispenser performance analysis. The performance analysis started with the preparation of the liquid to be used for the performance evaluation. A sugar solution with approximate viscosity as the methadone syrup is prepared to replace the methadone syrup if it cannot be used for the performance evaluation. Then, performance analysis is carried out by dispensing a specific amount of liquid for a number of runs by using the methadone dispenser and manual technique. The volume and dispensing time for both methods are recorded to be evaluated based on the accuracy, repeatability and dispensing time. The data obtained from the manual technique is provided by the healthcare practitioners from the treatment centre to ensure its accuracy. The methadone dispenser is also tested with different liquids to evaluate its efficiency. Once the data obtained is acceptable, data tabulation and discussion are carried out.

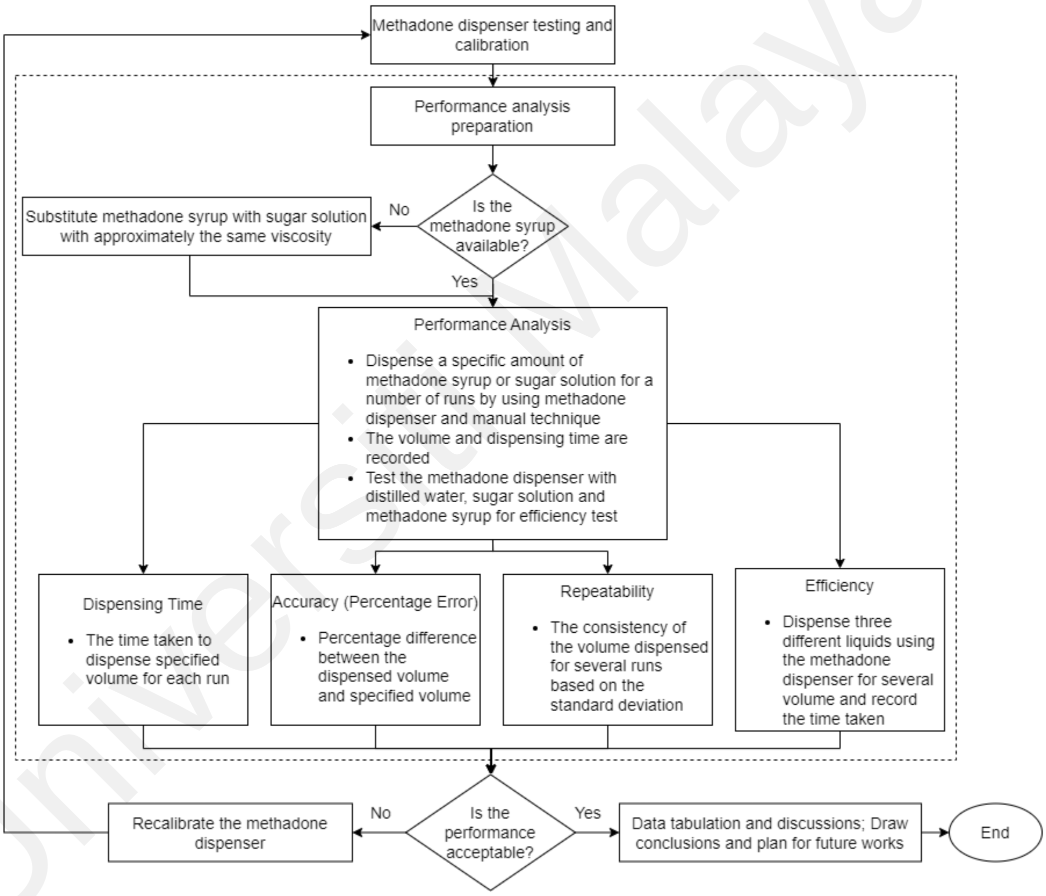

Figure 3.8 Detailed flowchart of methadone dispenser performance analysis

The automated methadone dispenser performance is evaluated and analysed based on several tests to ensure its functionality before it is applied in the local MMT centre. Tests that are done for product testing include accuracy and repeatability analysis. The efficiency analysis of the automated methadone dispenser is studied by using three types of solutions with different liquid properties such as viscosities and densities. The liquids used are methadone syrup, sugar solution and distilled water. Product testing was done to evaluate the dispensing process of the methadone syrup. The prescribed methadone conversion used is 5mg/ml which 1ml of methadone syrup contains 5mg of methadone. Based on the literature review, the amount of methadone dose used for the product test is 16ml (80mg) for 100 runs which is the common methadone dose administered daily (Petro et al., 2009).

3.4.1 Methadone Substitution Using Sugar Solution

Since methadone is a controlled drug and can only be handled and used by authorized medical professionals, the performance testing is substituted with a sugar solution that has approximate properties such as viscosity and density. This is because sugar solution contains carbohydrates as adjuvants with sucrose formula which is a viscosity enhancer (Jungen et al., 2013). Although Jungen et al. (2013) prepared a sucrose solution of 1mg/ml by dissolving 10mg of sucrose into 10ml of distilled water, a range of 1.2-1.4mg/ml is commonly used in pharmaceutical practices (Amran et al., 2019). Thus, to replace methadone syrup with a viscosity of 37.286mPa.s, a sugar solution with a concentration of 36.680mPa.s is used by dissolving 66.6mg of Bendosen sucrose in every 50ml of distilled water. The mixture was let to rest on the hot plate at 90°C as shown in Figure 3.9 to ensure the sucrose perfectly mixed with the distilled water.

Figure 3.9 Sugar solution on the hot plate at 90°C

Once the sugar solution is ready, SVM 3000 Starbinger viscometer was used to measure the dynamic viscosity. The dynamic viscosity of the sugar solution is taken several times at different temperatures to be compared with methadone syrup based on the literature review. Figure 3.10 shows the viscometer used to measure the viscosity of the sugar solution made.

Figure 3.10 SVM 3000 Starbinger viscometer used to measure the viscosity of sugar solution

3.4.2 Accuracy and Repeatability Analysis

The accuracy of the methadone dispenser is studied and analysed by dispensing sugar solution ranging from 2-50ml in increments of 2ml. Then, the data obtained is compared with the current method which is by using syringe and beaker. The results are also analysed by using the Pearson analysis to fully understand the relationship between the variables studied. The Pearson correlation coefficient represents the relationship between two variables, measured on the same interval and ratio scale. It measures the strength of the relationship between the two continuous variables. The Pearson coefficients are calculated by using the Equation (2) as shown below.

$$r = \frac{n(\sum xy)-(\sum x)(\sum y)}{\sqrt{[n\sum x^2-(\sum x)^2][n\sum x^2-(\sum y)^2]}} \qquad \text{Equation (2)}$$

where r = Pearson Coefficient

n = numbers of pairs of the data

$\sum xy$ = sum of products of the paired data

$\sum x$ = sum of data x

$\sum y$ = sum of data y

$\sum x^2$ = sum of squared data x

$\sum y^2$ = sum of squared data y

The accuracy of dispensing process was evaluated based on the percentage of error while the precision of the machine will be evaluated based on the repeatability of the dispensing process. Repeatability describes the proportion of the total distribution that is reproducible among the repeated measurements of the same subject or group within short time intervals (Nakagawa & Schielzeth, 2010). Error percentage and repeatability were calculated based on Equation (3) and (4) respectively.

$$\% \text{ Error} = [(\text{Theoretical} - \text{Experimental})/\text{Theoretical}] \times 100\% \qquad \text{Equation (3)}$$

$$\text{Repeatability}, \sigma_r = \sqrt{\sum(x_n - \bar{x})^2/(n-1)} \qquad \text{Equation (4)}$$

where $\bar{x}$ = mean volume dispensed,

x_n = volume dispensed at n^{th} run,

$\sum(x_n - \bar{x})^2$ = sum of squares of the difference between x_n and $\bar{x}$,

n = number of runs

The data for the accuracy and repeatability analysis is obtained by dispensing 16ml of sugar solution by using the methadone dispenser and manual technique for 100 runs. The sugar solution dispensed by the manual technique is carried out by one of the healthcare professionals to ensure that the data collected is not biased. The sugar solution dispensing process using the methadone dispenser is carried out by dispensing seven bottles simultaneously as shown in Figure 3.11. Then, the accuracy and repeatability of the two methods are compared and discussed. In this analysis, the research variables studied is the usage of different dispensing mechanisms which are syringe and beaker with peristaltic pump and load cell sensors and their effect on the volume of sugar solution dispensed as well as the time taken to dispense the sugar solution for a set volume.

Figure 3.11 Methadone dispenser sugar dispensing setup

3.4.3 Efficiency Analysis

The analysis of the efficiency of the automated methadone dispenser is carried out by dispensing three types of solutions with distinct liquid properties such as viscosities and densities. Three solutions that were used to evaluate the methadone dispenser are plain water, sucrose solution, and methadone syrup. In order to determine and verify the dynamic viscosity of each solution accurately, SVM 3000 Stabinger viscometer is used. Table 3.3 shows the properties which are concentration, dynamic viscosity, kinematic viscosity and density of methadone syrup, sugar solution and plain water.

Table 3.3 Methadone, sugar and water properties

Temperature [°C]	25		
Solution	Methadone	Sugar	Water
Concentration	5mg/ml	66.6g/50ml	1000mg/ml
Dynamic Viscosity, η [mPa.s]	37.286	36.680	0.889
Kinematic Viscosity, ν [mm²/s]	33.060	31.288	0.8926
Density, ρ [g/mm³]	1.158	1.277	0.997

The evaluation process for the efficiency of the automated methadone dispenser began by dispensing water using the automated methadone dispenser. Initially, 2ml of plain water is dispensed and it is repeated with 2ml increments until the cumulative volume of water that has been dispensed is 50ml. The time taken for the methadone dispenser to dispense the water for each 2ml increment is recorded. Next, the experiment and evaluation process is repeated for the remaining solutions which are sugar solution and methadone syrup. In this analysis, the research variable is the volumes dispensed by using syringe and beaker for manual technique as well as peristaltic pumps and load cell sensors for methadone dispenser. Volume dispensed and time taken for the dispensing process by both methods are recorded for different volumes dispensed ranging from 2ml to 50ml with 2 ml increment.

CHAPTER 4: RESULTS & DISCUSSIONS

4.1 Automated Methadone Dispenser

The isometric, side and rear views of the automated methadone dispenser are shown in Figure 4.1. Random dispensing processes were carried out and the methadone dispenser dispense the liquid accordingly. In addition, performance testing of the methadone dispenser was done to ensure its functionality and analyse the results. The automated methadone dispenser is designed and fabricated to fit the standard 1-litre methadone bottle container that is commonly used in health clinics and hospitals such as Adecure Syrup (*Adecure Syrup*, 2015). The seven custom-made bottle bases are designed and produced to fit the standard methadone prescription bottle that can be filled between 10-120ml.

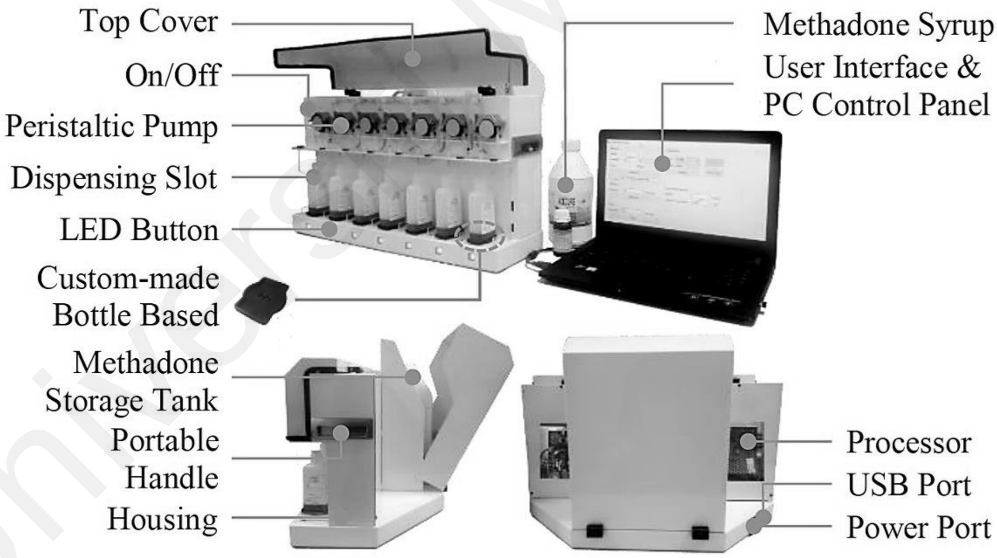

Figure 4.1 Isometric, side, and rear view of the automated methadone dispenser

The methadone dispenser as shown in Figure 4.1 uses peristaltic pumps as the dispensing mechanism. The peristaltic pumps used in the current research are also more compact and smaller than the diaphragm pump used in the previous research. The maintenance of the peristaltic pump is also easier as the tube is accessible and can be changed. Meanwhile, the maintenance of the diaphragm pump is more complicated as the pump needs to be disassembled to inspect the diaphragm. Besides, one study has found that a peristaltic pump allows a more regular flow and reduced level of noise and vibration, particularly at low and medium flow rates compared to a diaphragm pump (Longo et al., 2017).

The laptop interface as shown in Figure 3.7 allows the user to set the amount of liquid required and the dispenser will check the volume dispensed continuously by using the load cell sensors to ensure that it is accurate. Besides, the introduction of seven outlets allows the dispenser to dispense up to seven equal prescriptions simultaneously rather than dispensing the prescriptions one at a time using the device developed by Amran et al. (2019). Thus, the methadone dispenser is seven times faster as seven prescriptions can be dispensed simultaneously.

Another added feature of the newly developed dispenser is the liquid properties review and configuration. The user is able to check the current concentration and density of the liquid to ensure that it is the same as the storage. When the user inserted the required volume in ml, the algorithm will calculate the mass of prescriptions required based on the liquid properties as the dispenser is using load cell sensors. Besides, the newly developed methadone dispenser offers 3 options for the dispensing units which are gram(g), milligram(mg) and millilitre(ml) in case they are needed.

The dispenser is also equipped with a withdraw function where it will activate all the pumps in opposite direction to force all the remaining liquid along the tube into the storage. This will empty the tube and ensure that there is no wastage while reducing the risk of contamination. The user is only required to insert the duration of the withdrawal process as shown in the user interface in Figure 3.7.

Same to the withdraw function, the flush function requires the user to insert the duration only. The flush function is used when the user wants to clean the tube to remove any contamination. Before activating the flush function, the user is required to insert the inlet tube into cleaning liquid or distilled water. The flush tray needs to be inserted before the flushing process to ensure that the process can be carried out since there is an IR sensor that detects the tray to proceed with the flush function. Then all pumps will be activated at high speed to dispense the liquid through all outlets into the flush tray according to the duration set.

4.2 Methadone Substitution Using Sugar Solution

Methadone substitution using a sugar solution is carried out because methadone syrup is a controlled drug and cannot be obtained and used freely. The solution is prepared by dissolving 66.6mg of sucrose into 50ml of distilled water according to the literature review (Amran et al., 2019). Sucrose is also used to increase the viscosity during liquid methadone preparation while lactose is needed in pressing tablets (Jungen et al., 2013). Table 4.1 shows the dynamic viscosity of the sugar solution at different temperatures tested by using the SVM 3000 Stabinger Viscometer. The viscosity of the sugar solution is tested several times at four different temperatures and the best three were selected to obtain the average. This is because some of the data obtained fluctuated, which affects the accuracy. Thus, to ensure the consistency and accuracy of the data, three sets of readings with similar reduction patterns were selected.

Table 4.1 Dynamic viscosity of sugar solution at different temperatures

Temperature [°C]	Dynamic Viscosity, η [mPa.s]			
	Reading 1	Reading 2	Reading 3	Average
20	44.561	45.162	43.098	44.274
22	40.721	41.048	39.203	40.324
25	39.973	36.938	33.129	36.680
37	21.971	19.666	19.650	20.429

Based on the viscosity obtained, the viscosities of the sugar solution were compared with the viscosities of methadone syrup at the same temperature as reported by Amran et al. (2019). Table 4.2 shows the viscosities of the sugar solution and methadone syrup at different temperatures. Since the experiment is conducted at room temperature which is approximately 25°C, the viscosities of both solutions at 25°C are compared, and it is found that the percentage of difference is 1.625% which is acceptable. The sugar solution then is used for methadone dispenser performance evaluation. The slight difference is due to the sucrose to water ratio which produces the smallest difference as the viscosity values are mili-Pascal.second (mPa.s).

Table 4.2 Dynamic viscosity of methadone syrup and sugar solution at different temperatures

Temperature [°C]	Dynamic Viscosity, η [mPa.s]	
	Methadone 5mg/ml	Sugar Solution 66.6mg/50ml
20	44.733	44.274
22	41.451	40.324
25	37.286	36.680
37	29.211	20.429

Another study has also prepared a sugar solution by dissolving 10mg of sucrose in 10ml of distilled water (Jungen et al., 2013). The study does not include the viscosity of the solution prepared since they are evaluating the sugar amount when digested instead of testing the solution. However, the concentration that they used is still in the range generally used in pharmaceutical practices (Amran et al., 2019). Thus, the sugar solution prepared is suitable to be used in the testing and performance analysis as methadone substitution.

4.3 Performance Evaluation

4.3.1 Accuracy and Repeatability Analysis

The automated methadone dispenser was evaluated by dispensing the sugar solution with an increment of 2ml for 25 runs until the cumulative volume that has been dispensed is 50ml. The volume and time taken for each run were recorded and compared with the manual method. Figure 4.2 shows the volume dispensed over time by both techniques where the volume dispensed increases at a different rate as the time increases. For similar volume and increment, the volume dispensed by the methadone dispenser increased faster in a shorter dispensing time whereas a longer and more inconsistent liquid dispensing process is shown by the manual technique. The total time taken to dispense 50.30ml of liquid is 57s whereas the total time required to dispense 52ml of liquid manually is 349.32s. Based on these values, the methadone dispenser has reduced the %Error from 4% to 0.6% and dispensing time by 83.68%.

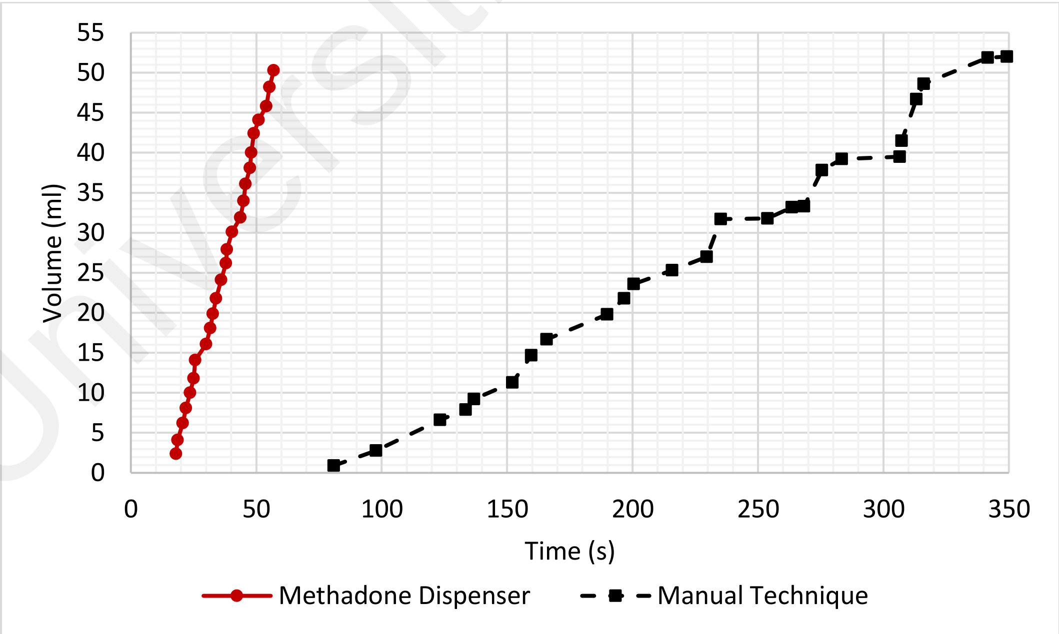

Figure 4.2 Volume dispensed over time for manual technique and methadone dispenser

Based on the gradient of the trendline for both methods, the average flow rate of the methadone dispenser and manual technique is 1.21ml/s and 0.2ml/s respectively. This shows that the flow rate of the methadone dispenser to dispense a total of 50ml of liquid is approximately six times faster than the manual technique. The larger margin of error in the volume dispensed manually compared to the automated methadone dispenser is also caused by the limited human capability (Amran et al., 2019). Thus, the limited human capability in the manual technique has led to a longer time taken to dispense and a larger error margin in the volume compared to the automated methadone dispenser.

Figure 4.3 shows the volume dispensed for 25 runs for manual technique and methadone dispenser according to the prescribed doses while Figure 4.4 shows the time taken for the dispensing process for each run by manual technique and methadone dispenser. A line is drawn for the ninth run in Figure 4.3 and Figure 4.4 to compare and evaluate the volume dispensed and the time taken by both techniques. Based on the graphs, the manual technique dispensed 19.8ml in 189.90s, whereas the methadone dispenser dispensed 18.1ml in 31.67s. By using the formula in Equation 1, the methadone dispenser shows an improvement of % Error from 10.00% to 0.71% and an improvement in dispensing time by 83.32%. Based on the average, the % Error is reduced from 8.58% to 1.50%. This shows that the automated methadone dispenser is able to dispense the prescribed dose with a lower % Error in a shorter time compared to the manual technique.

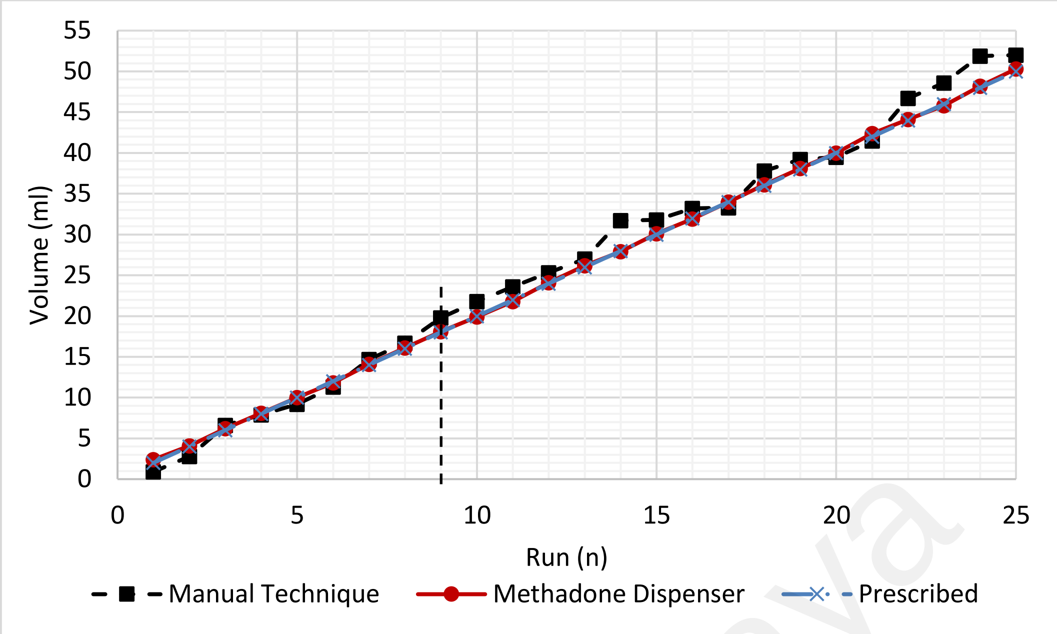

Figure 4.3 Volume dispensed for 25 runs for manual technique and methadone dispenser according to the prescribed doses

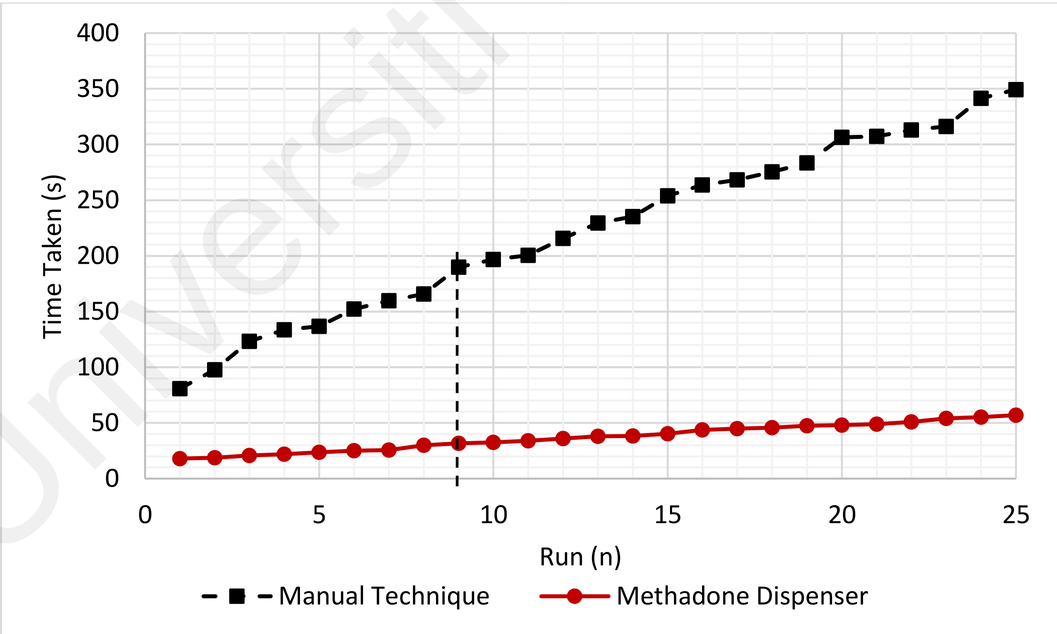

Figure 4.4 Time taken for the dispensing process for each run by manual technique and methadone dispenser

Based on the data obtained for both methadone dispenser and manual technique, the Pearson analysis is carried out. By using Equation (1), the Pearson coefficient obtained for methadone dispenser and manual technique is 0.998 and 0.994 respectively. Based on the values, it is found that the methadone dispenser has a slightly stronger positive correlation compared to manual technique. The positive coefficient for both methods show that the data are directly proportional to each other.

The performance of the automated methadone dispenser was then evaluated based on repeatability (σ_r) as shown in Equation 2 to determine the effectiveness of the methadone dispenser (Zhang, 2014). Besides, σ_r is an important parameter in evaluating the consistency (Amran et al., 2019). In this research, the σ_r provides an approximation of the capability of the methadone dispenser to facilitate repeatability of dispensing methadone syrup with specific concentrations.

The methadone dispenser is also tested to dispense 16ml of sugar solution which is the commonly prescribed dose among patients (Petro et al., 2009). The volume dispensed by each outlet was recorded for 100 runs and compared with the manual technique. The maximum and minimum volume dispensed for each outlet and methods are tabulated to calculate the range of % Error. Besides, based on the first 100 data obtained for both the methadone dispenser and manual technique, the repeatability is calculated based on the standard deviation.

Table 4.3 shows the percentage error for the manual technique and methadone dispenser while Table 4.4 shows the repeatability for the manual technique and methadone dispenser. The tabulated data shows that greater consistency of volume dispensed by automated methadone dispensers led to smaller % Error and σ_r compared to the manual technique. Besides, the methadone dispenser has a smaller % Error range and σ_r compared to the manual technique which is based on the smaller deviation of the volume dispensed. The volume dispensed by the manual technique for 100 runs ranges between $15.3 \leq$ Volume (ml) ≤ 17.4 with a maximum % Error of 8.75% while the volume dispensed by the automated methadone dispenser ranged between $15.6 \leq$ Volume (ml) $\leq$

16.6 with the maximum % Error of 3.75%. This indicates that the usage of the automated methadone dispenser has led to a reduction in errors.

Table 4.3 Percentage errors for the manual technique and methadone dispenser

Bottle Slots	Manual Technique				Methadone Dispenser			
	Volume (ml)		Error (%)		Volume (ml)		Error (%)	
	Min.	Max.	Min.	Max.	Min.	Max.	Min.	Max.
1	16.4	17.1	2.50	6.88	15.6	16.5	2.50	3.13
2	15.7	17.0	1.88	6.25	15.7	16.5	1.88	3.13
3	15.4	17.4	3.75	8.75	15.7	16.6	1.88	3.75
4	15.7	17.3	1.88	8.13	15.8	16.6	1.25	3.75
5	15.6	17.3	2.50	8.13	15.7	16.5	1.88	2.13
6	15.3	17.0	4.38	6.25	15.7	16.6	1.88	3.75
7	15.8	17.0	1.25	6.25	15.7	16.6	1.88	3.75
Range	15.3 ≤ Volume ≤ 17.4		1.25 ≤ Error ≤ 8.75		15.6 ≤ Volume ≤ 16.6		1.25 ≤ Error ≤ 3.75	

Table 4.4 Repeatability for the manual technique and the methadone dispenser

n = 100	Manual Technique		Methadone Dispenser	
	Volume (ml)	Time Taken (s)	Volume (ml)	Time Taken (s)
Mean, $\bar{x}$	16.70	165.78	16.06	30.36
Sum of Squares, $\sum(x_n - \bar{x})^2$	7.0584	501.16	2.7036	43.04
Repeatability, σ_r $\sqrt{\frac{\sum(x_n-\bar{x})^2}{n-1}}$	0.267	2.250	0.165	0.659
Remarks	Based on the average data, • The usage of the methadone dispenser has reduced the dispensing time by 81.69% compared to the manual technique. • The usage of the methadone dispenser has improved the accuracy by 4.0% compared to the manual method.			

Based on the performance evaluation done, the automated methadone dispenser managed to improve the accuracy and dispensing time by 4.0% and 81.69% respectively. The volume dispensed manually ranges between 15.3 ≤ Volume (ml) ≤ 17.4 with error ranges between 1.25 ≤ Error (%) ≤ 8.75 while the volume dispensed by the methadone dispenser ranges between 15.6 ≤ Volume (ml) ≤ 16.6 with error ranges between 1.25 ≤ Error (%) ≤ 3.75. On average, the percentage error is reduced from 8.58% to 1.50%. This shows that the automated methadone dispenser is able to measure and dispense the specified dose with a lower % Error and faster dispensing time compared to the manual technique.

Based on Table 4.4, the repeatability obtained to dispense an average of 16.06ml by using the methadone dispenser is 0.165 while the repeatability obtained to dispense an average of 16.70ml of liquid by using the manual technique is 0.267. This shows that the methadone dispenser is more consistent since it has a smaller deviation from the mean values with a more accurate average dispensing volume compared to the manual technique.

Compared to Amran et al.(2019) who tested the dispenser by dispensing 104mg of liquid, the methadone dispenser was able to dispense liquid with a mean volume of 104.367mg and repeatability of 1.246. Meanwhile, the manual technique which has a mean value of 108.564 produce a repeatability of 1.266 (Amran et al., 2019). Another study was carried out in which they tested the prototype that was developed in several treatment centres (Vahidreza & Manouchehr, 2019). In this study, they have found that the mean and standard deviation of the error of the device is 0.232 $\pm$ 0.055ml with a relative error of 1.33 $\pm$ 0.58%. This shows that the device developed has the smallest sensitivity of 0.177ml. Thus, the usage of methadone dispensers has been proven to be able to improve the consistency and accuracy of the volume dispensed.

Furthermore, the methadone dispenser produced smaller σ_r which is associated with relatively higher repeatability and better precision than the manual technique. A smaller repeatability value results in a smaller deviation of the data from the mean value.

Figure 4.5 shows the volume dispensed by manual technique for the first 50 out of 100 runs into seven prescription bottles. The graph shows that most of the volume dispensed is greater than the prescribed volume which is 16ml which is shown by the dashed line. The data distribution shows that approximately 95.71% of the volumes dispensed are between 16.4ml and 17ml. Besides, no volume within 0.1ml of the prescribed volume is recorded for the manual technique. This shows that the current manual technique is having difficulties following the necessary accuracy standard which is mainly might be caused by the human capability limitations and the lack of measuring precision based on the syringe gradations with a range of error less than 1.0ml (Amran et al., 2019).

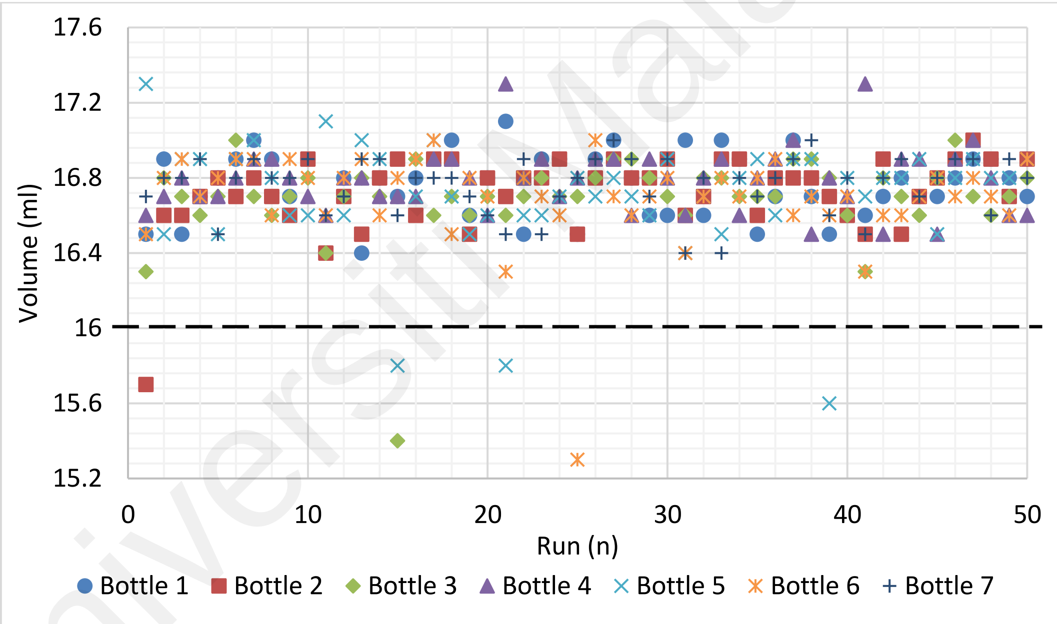

Figure 4.5 Volume dispensed for 50 out of 100 runs for seven prescription bottles by manual technique

Meanwhile, Figure 4.6 shows the volume dispensed for 50 out of 100 runs for seven prescription bottles by methadone dispenser. Based on the plots, around 66.0% of the volumes dispensed are within ±0.1ml of the prescribed dose. Besides, all the volumes that were dispensed are within ±1.0ml of the prescribed dose. The results show that the volume dispensed by the automated methadone dispenser is within the allowable range and smaller compared to the manual technique (Amran et al., 2019). Thus, the methadone dispenser provides more accurate dosing with a smaller range of deviations to the patients as the result of accurate critical mechanical components application.

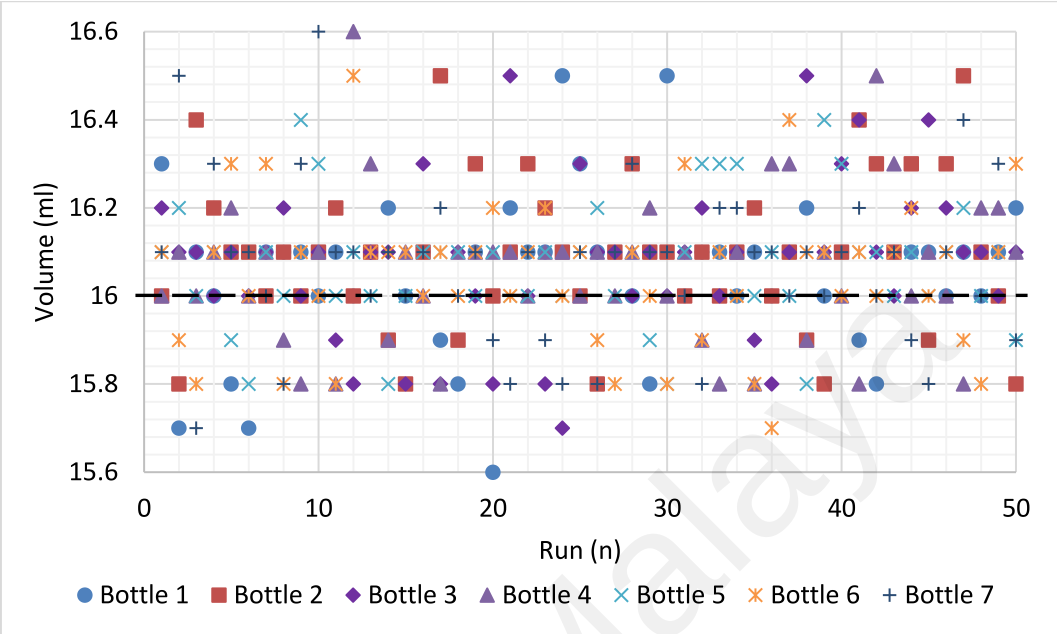

Figure 4.6 Volume dispensed for 50 out of 100 runs for seven prescription bottles by methadone dispenser

The comparison between the volume dispensed and dispensing time for the manual technique and methadone dispenser are shown in Figure 4.7 and Figure 4.8 respectively. A line is plotted on the 50th run of the liquid dispensing process in each graph to compare the volume dispensed and the time taken to dispense the respective volume. The graphs show that the automated methadone dispenser dispensed 15.9ml in 31s while the manual technique dispensed 16.9ml in 163s. The flow rate to dispense the respective volume for the methadone dispenser and manual technique is approximately 0.513ml/s and 0.104ml/s respectively. Thus, the findings show that the automated methadone dispenser is not only able to improve the dispensing accuracy but also dispense faster which leads to reduced dispensing time.

The shorter time taken by the automated methadone dispenser to dispense methadone syrup reduces human needs for resources and therefore improves the efficiency of both the prescription delivery system and patient care (Noparatayaporn et al., 2017). Thus, the methadone dispenser is proven to be feasible and reliable for the current clinical practices of the methadone syrup dispensing process for drug addiction therapy.

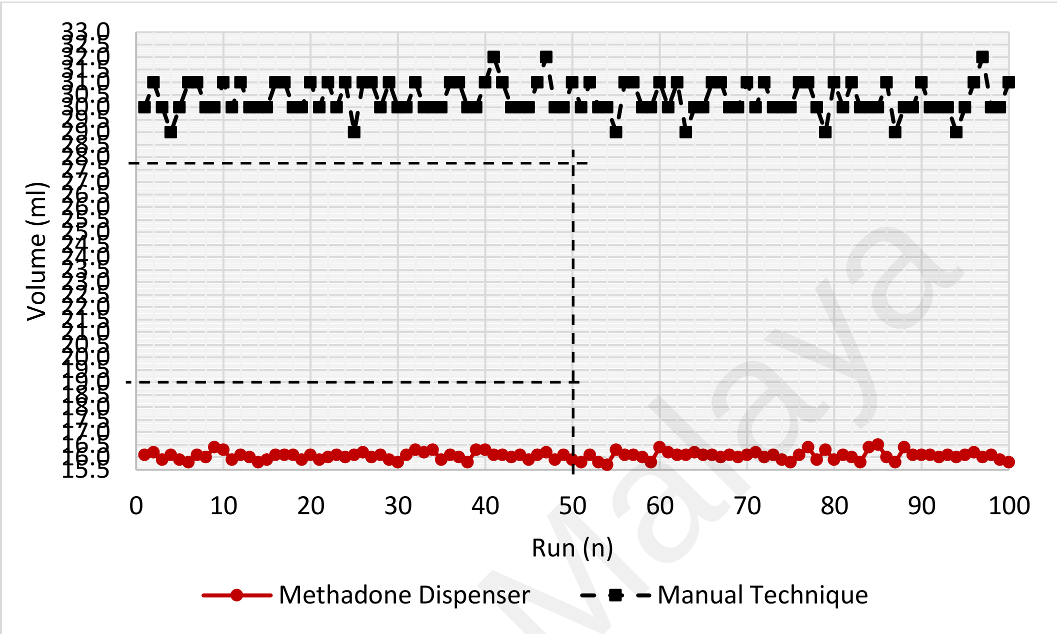

Figure 4.7 Comparison between volume dispensed at 16ml for 100 runs by using manual technique and methadone dispenser

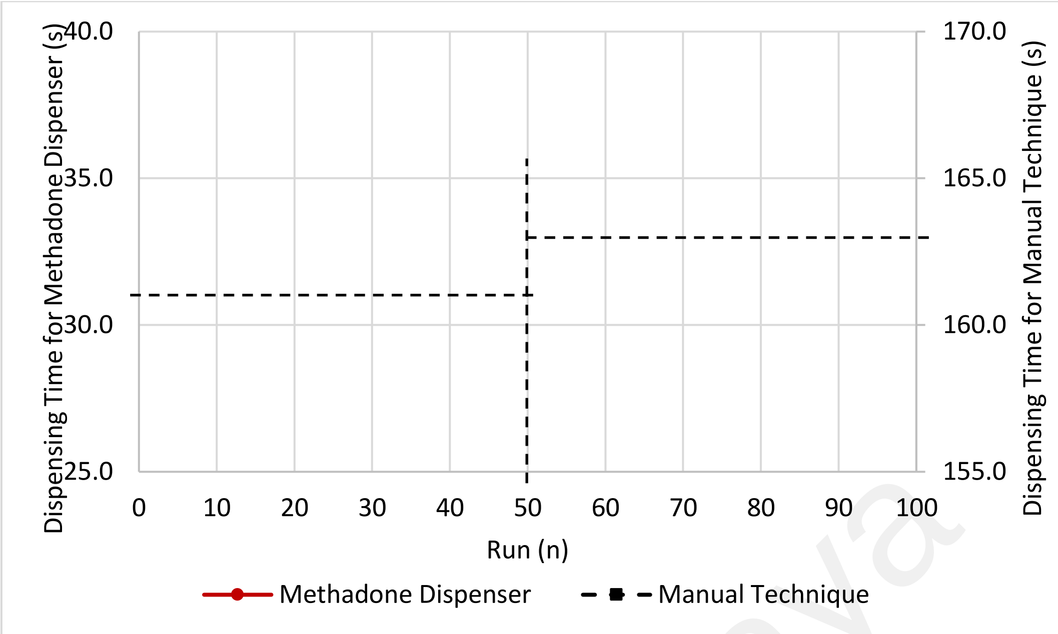

Figure 4.8 Comparison between the time taken to dispense 16ml of fluid for 100 runs by using manual technique and methadone dispenser

4.3.2 Efficiency Analysis

Figure 4.9 shows the volume dispensed for different liquids over time by using the automated methadone dispenser. The graph shows that the volume dispensed ranges between 2-50ml with an increment of 2ml. For example, the volume of water dispensed at 30, 40 and 50s is higher than both sugar solution and methadone syrup at the respective time. The water has a higher flow rate compared to the other two liquids since water has a lower viscosity than sugar solution and methadone syrup as tabulated in Table 3.3. This shows that a low-viscosity liquid such as water can flow easier and faster than a high-viscosity liquid due to less power needed by the pump to dispense the liquid leading to a higher flow rate.

Meanwhile, the volume of sugar solution and methadone is gradually increasing at an almost similar rate. The small difference in the volume dispensed for sugar solution and methadone syrup at any instantaneous time is because of the approximate viscosity causing them to experience similar flowability. This shows that high-viscosity solutions such as methadone syrup and sugar solution require a longer dispensing time compared to lower-viscosity solutions. This is because as the viscosity increases, the flow rate decreases when other parameters are maintained (Abd El Naby et al., 2004). Thus, this proves that the dynamic viscosity is inversely proportional to the volumetric flow rate as shown in Hagen–Poiseuille equation in Equation (1).

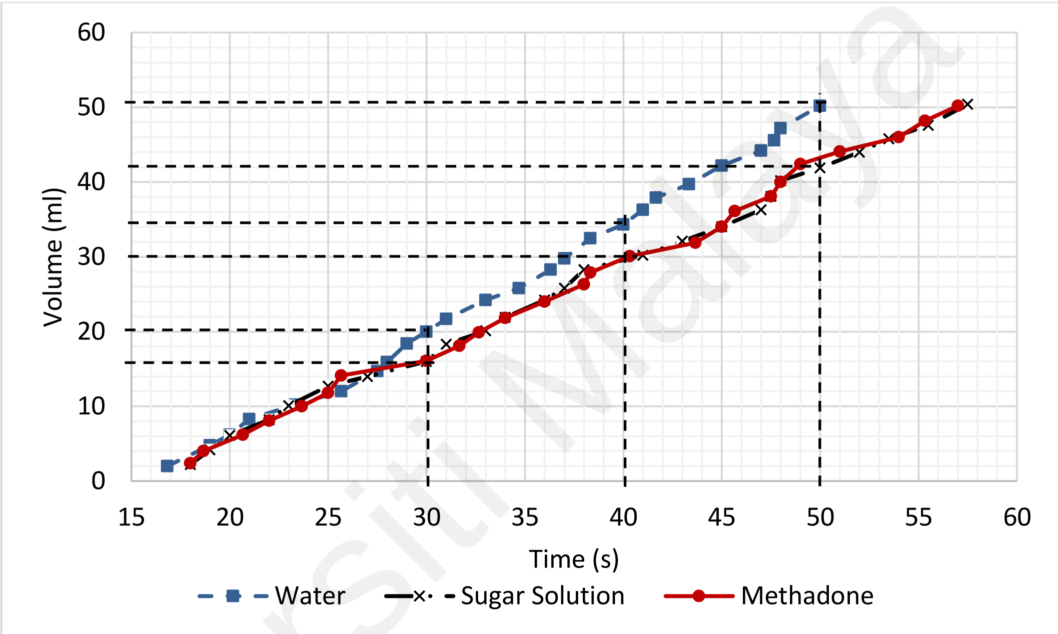

Figure 4.9 Comparison between the volume of different liquids dispensed over time by using the methadone dispenser

CHAPTER 5: CONCLUSIONS & RECOMMENDATIONS

5.1 Conclusions

In this research, an automated methadone dispenser equipped with seven outlets is developed and tested. The dispenser can dispense the required volume specified in the program embedded in the laptop. The additional functions which are Withdraw and Flush can also be carried out by the dispenser. The performance of the methadone dispensers is studied. Sugar solution has been successfully prepared by dissolving 66.6mg of sucrose into each 50ml of distilled water as methadone syrup substitution with dynamic viscosity of 36.680mPa.s and percentage error of 1.625%. The sugar solution is dispensed from 2-50ml in increments of 2ml by using the methadone dispenser and manual technique. Based on the Pearson analysis done, it is found that the Pearson coefficient for methadone dispenser and manual technique is 0.998 and 0.994 respectively. This shows that the methadone dispenser has stronger positive correlation. The % Error, dispensing time, and accuracy of the automated methadone dispenser was measured by dispensing 16ml (80mg) of sugar solution for 100 runs. In summary, the usage of the automated methadone dispenser reduces the % Error from 8.58% to 1.50% and improves the dispensing time by 81.69%. The automated methadone dispenser also increased the dispensing accuracy by 4.0%. Thus, the findings show that the automated methadone dispenser that has been developed is highly reliable and feasible, especially in the reduction of errors in dispensing process which can ensure a safe methadone syrup intake among patients. The implementation and usage of the automated methadone dispenser in the pharmacy and treatment centre could help in reducing and improving the health practitioner’s workflow. Furthermore, the automated methadone dispenser can help pharmacists in dispensing methadone efficiently in the MMT program.

5.2 Study Limitations

The main constraint of the study is the availability of methadone syrup to be used in the performance evaluation. This is because as stated in the methodology section, methadone syrup is a controlled drug and can only be handled by healthcare professionals such as pharmacists. Although the methadone syrup has been substituted with sugar solution with approximate properties such as viscosity, it is still not 100% identical which might cause slight deviation in the results obtained.

Next, the accuracy and consistency of the data obtained from the manual technique such as volume dispensed and time taken will highly differ based on the person conducting the dispensing process. This is because different people have different capabilities and accuracy in dispensing methadone syrup repeatedly. To ensure the consistency and accuracy of the data, one healthcare professional who is normally in charge of dispensing methadone syrup is chosen to dispense the liquid for 100 runs.

Another limitation when conducting the study is the lack of research and development done on automated methadone dispensers. This is because the innovation can be considered new as most of the dispensing processes of the MMT program are being done manually. This limitation prevented more detailed comparisons to be carried out to study the performance between different methadone dispenser. Besides, there is less emphasis on improvement and innovation in terms of a medical device for the MMT program. Thus, there is a lack of research done on the methadone substitution and performance analysis of methadone dispensers. However, some researches are viable and can be reviewed and included in this research.

5.3 Future Recommendations

For future research, the database in a web application can be integrated with the automated methadone dispenser to enhance the whole MMT program and eliminate the need for reviewing, tracking and updating records manually. As for the automated methadone dispenser, a diluting system can be introduced and equipped to improve the overall prescription performance and efficiency as currently the methadone syrup is being diluted. The tubing system of the methadone dispenser can also be studied and improved to ensure that the methadone dispensing process is uniform and consistent at all outlets.

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