

FORMULATION OF GEL HAND SANITIZER
USING RESPONSE SURFACE METHODOLOGY

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I/We* hereby declare that I/We* have checked this thesis/project* and in my/our* opinion, this thesis/project* is adequate in terms of scope and quality for the award of the degree of Bachelor of Manufacturing Engineering Technology (Pharmaceutical).

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I hereby declare that the work in this thesis is based on my original work except for quotations and citations which have been duly acknowledged. I also declare that it has not been previously or concurrently submitted for any other degree at University Malaysia Pahang or any other institutions.

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ABSTRAK

Pembersih tangan adalah satu satu cara atau teknik penjagaan kebersihan yang perlu dititikberatkan pada masa kini. Pelbagai jenis penyakit kulit seperti kudis, alergik dan ruam kini makin menular dalam kalangan masyarakat melalui sentuhan, peralatan rumah dan sebagainya. Dengan adanya satu inovasi pembersih tangan yang baru tanpa menggunakan sabun dan air, mampu menjimatkan masa dan memberikan kemudahan kepada para pengguna. Oleh kerana itu, suatu kajian mengenai penciptaan formulasi yang baharu telah dijalankan untuk menentukan pengoptimum yang terbaik dalam mencipta pembersih tangan yang berasaskan ekstrak herba daun sirih. Teknik rekabentuk *D-Optimal* (DO) melalui Kaedah Tindak Balas Permukaan dalam perisian *Design Expert* telah digunakan untuk menentukan keadaan yang terbaik dalam penghasilan formulasi yang paling sesuai. Antara faktor yang digunakan adalah nisbah Isopropil alkohol dan ekstrak daun sirih. Diameter zon perencatan bakteria merupakan tindak balas yang menjadi pengukur keberkesanan antara campuran Isopropil alkohol dan ekstrak daun sirih. Dalam pada itu, perisian Kaedah Tindak Balas Permukaan akan memberikan nilai-nilai penting yang diperlukan dalam proses pengoptimuman melalui set data yang telah ditentukan. Setiap aktiviti eksperimen adalah berdasarkan set data yang disediakan. Teknik Agar Penyebaran telah dipilih sebagai kaedah untuk kerja-kerja eksperimen. Nilai yang diukur berdasarkan pemerhatian eksperimen akan digunakan sebagai jumlah sebenar tindak balas. Keputusan analisis varians iaitu (ANOVA) akan diinterpretasikan sebagai inferens untuk mencapai setiap objektif yang dibincangkan melalui pemilihan julat nisbah Isopropil alkohol dan ekstrak daun sirih. Berdasarkan analisis yang ditunjukkan menerusi Kaedah Tindak Balas Permukaan, keadaan optimum julat nisbah Isopropil alkohol dan ekstrak daun sirih untuk pengoptimuman formula baru ialah 63%. Secara keseluruhannya, keputusan ini menunjukkan bahawa formulasi Isopropil alkohol baru akan memberi kesan yang terbaik dengan nisbah yang lebih tinggi berbanding bahan-bahan aktif seperti mengelakkan daripada berlaku merengsa kulit dan mudah meruap yang menyebabkan kurang kecekapan.

ABSTRACT

Hand sanitizer is introduced as a new alternative way in hand hygiene technique that should be noted among people nowadays. Variety types of skin diseases such as psoriasis, rashes, impetigo and cellulitis are easily get transferred via skin contact, household appliances and many more. New invention of sanitizer is preferable due to its advantages that convenient and save time give a good impact for the consumers compared to hand washing and soap. Due to that case, a research regarding on determining a formulation has been done in order to investigate the best optimization based on alcohol based hand sanitizer with herbal traditional extract. D-Optimum Design (DO) technique via Response Surface Methodology in Design Expert Software is used to justify the most suitable condition in order to create an appropriate formulation. Some factors that been used are the ratio between the main Active Pharmaceutical Ingredient, (API) Isopropyl alcohol and piper betel extract. Zone inhibition diameter is used as the indicator to detect the effectiveness between combination of Isopropyl alcohol and piper betel extract towards antimicrobial activity, Gram-Positive bacteria and Gram-Negative bacteria. The values interpreted from Response Surface Methodology are acquired to assist in optimization process throughout a set of data. All the tasks in this experiment are based on the set data given. Agar Well Diffusion method is choose to investigate the effectiveness of each formulation by observing the antimicrobial activity. The results obtained from (ANOVA) will be discuss to make inference in order to achieve the objectives of this research upon selected best ratio of Isopropyl alcohol and Piper betel extract. According to analysis interpreted from Response Surface Methodology, the value ratio of Isopropyl alcohol and Piper betel extract is lie between 63%, validated as the best optimization. In overall, this result depicts that determination value of ratio for Isopropyl alcohol will give a great impact within suitable value ratio compared to the excipients such as can prevent from skin irritation and easy to evaporated, lead to low of sensitivity reaction.

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LIST OF SYMBOLS

cm	Centimeter
°C	Degree celcius
g	gram
L	liter
m ²	metre square
μl	microliter
ml	mililiter
mm	millimeter
nm	nanometer
%	percentage
w/v	Weight per volume
w/w	weight per weight

LIST OF ABBREVIATIONS

AI	Active ingredients
API	Active Pharmaceutical Ingredients
rpm	Rotation per minute

CHAPTER 1

INTRODUCTION

1.1 Background of study

First influenza disease that happened throughout in September 2013 recognized as a crucial issue which resulting to 28,368 cases, 11,316 deaths and establishing the disease as endemic in the region. Recently, it has been spread slowly to Malaysia's citizen due to the migration people from the outside country. Based on the statistical data from World Health Organization and National Health, patients that been infected by this kind of disease have increased year by year from 22.3% to 27.5% (Prakash, 2015). It was first identified in rural areas due to high number of patients admitted in the hospital that caused by skin diseases (Prakash, 2015). The statement was supported by (Hong, Clauson and Prochnow, 2016) since the problem was not a rare case mostly for adults and children. Hands is the main transmission modes of getting contaminated through skin contact. The bacteria that particularly cause this kind of disease were the gram-positive bacteria such as *Staphylococcus aureus* and *Bacillus subtilis* (Reynolds, Levy and Walker, 2006).

The Gram-positive bacteria usually have a high potential that lead to serious skin diseases, like Cellulitis causes a painful, red infection that is usually warm to the touch. As stated by (Cox, 2016), Cellulitis mostly occurs often on the legs, but it can appear anywhere on the part of body. Infection of hair follicles that causes red, swollen bumps like pimples was caused by folliculitis. Impetigo was also a very bad skin disease because there were present of oozing sores that bullous form of impetigo causes large blisters while the non-bullous form has a yellow, crusted appearance.

As those types infections shows that they were very easily got spread by the bacteria through contacts and air surroundings, Louis (2003) reported that the sources of

infection should be clarified and diminished it immediately before the things getting more worse in order to overcome the problem.

Hand washing is declared as the best way to ensure the hands were clean from bacteria, microbes and dirt. However, the problems regarding skin infections and illness among people remains since that most of them are not really concerned about the behavior of hand washing itself. Not only that, the factors of the problem also has been identified due to difficulties in water availability mostly for workers in construction site (Pickering et al., 2010). Therefore, in order to make it more convenient for people usage, the presence of new hand antiseptic interventions was introduced as an alternative way or as a supplement to hand washing with soap and water. The forms of hand sanitizer product can presence in such as foams, gels and also in liquid. The main Active Pharmaceutical Ingredients (API), of sanitizer, known as alcohol has a higher ability to possess antimicrobial activity.

Boyce (2013) in his research revealed that the optimum range of alcohol used to ensure its effectiveness towards antimicrobial activity within pH 6.8-7 was about 60-70% from overall ingredients. Apart from that, there were also presence of other kinds of hand sanitizer such as non-alcohol and alcohol with plant extract. Selection of alcohol with herbal plant extract has determined as best product one compared to contain only alcohol. This is because traditional healers from herbal plant extract can prevent and cure infectious condition and has low side effects to the consumer which is very rare in cases (Dixit et al., 2014). Hence, Piper betel (betel plant), are chosen to be the ingredients used in the formulation of herbal hand sanitizer. Betel plant is one of the rich plant species that has high resistant towards microbial activity and act as antioxidant. As it has been eloquently stated, this study seeks to analyze the evaluation of herbal hand sanitizer comprising alcohol extract combination with astonishing herbs using other suitable excipients which can be used as ready to use herbal hand sanitizer.

Ranade and Thiagarajan (2017) mentioned that Response Surface Methodology is a term applied function to multivariate techniques that can generate response surface and provide optimal solutions. Most of critical process in industry need to optimize its condition by referring to the selection of parametric conditions either the response is maximized or minimized. This method can related to this issue arise which in order to

create a best formulation of gel hand sanitizer, the process need a optimum condition so that the production timeline will save more, along with lower cost consumption. Besides that, it able to assist during the process undergoing to attain a best system performance.

1.2 Problem statement

Germs are easily get spread through transmission modes like skin contact and through opening such as the nose, mouth and also via breaks in the skin. Not only that, big exposure condition like electrical appliances or household items are also one of the sources of bacteria contagious. Those factors are leading to several disease like septic arthritis, toxic shock syndrome and septicemia that mostly caused by bacteria *Staphylococcus aureus* (Otto, 2011). Thus, in order to overcome this health problem, new invention of gel hand sanitizer is one of the ideas generated by Joe Kanfer, a CEO of hand soap company in Ohio, Japan. According to (Owen, 2013), he reveals that Kanfer decided to create an alternative way of hand care technique by optimizing the uses of applicable alcohol into making a sanitizer. As there are various types of alcohol available, Kanfer determined to choose isopropyl alcohol or commonly known as isopropanol, because it is one of the agents that able to inhibit the growth and development of bacteria on human skin. In this research, the gel hand sanitizer is going to be formulated with combination of Active Pharmaceutical Ingredient (API) between isopropanol and Piper betel extract. Since there are variety types or brands of hand sanitizer marketed, yet the concentration of isopropanol need to be justified before deciding the exact amount of uptake due to its limitation that the higher the concentration of alcohol beyond the standards, will cause irritation to skin and corrosiveness. Other than that, due its physical properties, it might be easy to volatile and this type of problem can affect the effectiveness of hand sanitizer that inversely proportional with time. Hand sanitizer is extensively used in office, homes, schools and also other healthcare places intended for topical application

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