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Software Development EXC-Sol as Supporting Suspension Dosage Pre-formulations

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ABSTRACT
In designing a drug dosage, required additional materials appropriate selection in the formulation. It is not desirable in case of incompatibility because it will produce a preparation quality is not good. The purpose of this research is to design software algorithms capable of analyzing the incompatibility of an additive based on incompatibility data in the handbook of pharmaceutical excipients 6 edition accompanied by a description of the material features and feature restrictions concentration. This software is called EXC-Sol. After the simulation, EXC-Sol capable to designing 35 of suspension formula by different suspending agents in each formula. The simulation results have been compared with the source incompatibility data for validation and the results did not show any material information that is incompatible in the 35th formula EXC-Sol simulation results.
Keywords: *EXC-Sol, incompatibility, suspension.*

1. Introduction

The design of an appropriate dosage form requires consideration of the characteristics of physical, chemical, and biological materials from all the drugs and pharmaceutical ingredients to be used in making the product. Drug and pharmaceutical ingredients used must be mixed with one another to produce a drug product that is stable, effective, attractive, easy to make and safe (Allen, 2013).

Pre-formulation data collected and studied from a variety of available libraries. The more complete the data collected will further facilitate the formulation. With complete data, the formulation can be made more precise, accurate, effective, and efficient in order to meet the objective of making the pharmaceutical preparations are physicochemical and bio-pharmaceutical good (Kurniawan, 2013).

There are many books or e-books that can be used to collect data characteristics of the physico-chemical (stability, incompatibility, description, solubility, pH, molecular formula, molecular weight and concentration of materials) of which is the Handbook of Pharmaceutical excipients 5th edition (2006) and the 6th edition (2009) and the Indonesian Pharmacopoeia 3rd edition (1979) and the fourth edition (1995). Martindale Edition 36 (2009) and the Handbook of Pharmaceutical Manufacturing Formulation Volume 3 (2004) are among the as a source of information to determine the nature of the active substance as well as a good way of processing. In the selection of

additional materials pharmaceutical preparation is not done randomly, but require carefulness in analyzing the data incompatibility, stability, and solubility of the material so that the problem often encountered is the difficulty of adjusting the additional materials to one another without being incompatible or affect the stability of the drug and other additives.

The suspension is a liquid preparation containing insoluble solid particles are dispersed in the liquid phase (Direktorat Jendral POM, 2014). Harder liquid preparation is formulated and maintained its stability compared with solid dosage (Allen, 2013).

It is what lies behind the researchers developed a software named EXC-Sol. EXC-Sol made using BASIC language that will be composed of some of the features of which is a feature incompatibility analysis, concentration calculation features, and features material descriptions of mutual support for the design of the suspension dosage formula.

2. Methods

Tools and Materials

Laptop ASUS Intel® Core™ i5-4200U CPU @ 1.60GHz 2.30 GHz, Microsoft Visual Studio 2015, Mouse, Wifi, Microsoft Office Access 2016, E-book Handbook of Pharmaceutical Excipients 5th Edition, E-book Handbook of Pharmaceutical Excipients 6th Edition, Indonesian Pharmacopoeia 3rd Edition, and Indonesian Pharmacopoeia 4th Edition.

Making Software EXC-Sol

Data Collection

1) In making the software EXC-Sol necessary data is information regarding incompatibility, stability, solubility, descriptions, pH, usability, and the concentration of material. Such information can be found in the e-book Handbook of Pharmaceutical excipients 5th edition and the 6th edition, as well as in the Indonesian Pharmacopoeia 3rd Edition and the 4th edition.
2) Conversion Algorithm to BASIC language

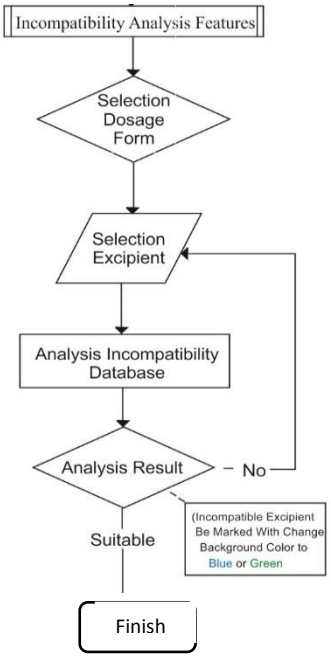


Figure 1 Algorithm IncompatibilityAnalysis Features

In the analysis features incompatibility, instantly analyzes whether there is any material that is incompatible, and change the background color in blue and green if there are incompatible materials. Incompatible materials can be replaced with a selection of existing materials so that formulators can get a formula that fits easily. In this feature, the dosage form is designed subprogram his suspension. This feature is made in the form of lists for each function of the material so that formulators more easily choose the materials.

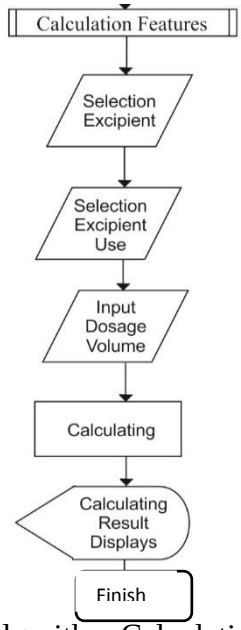


Figure 2. Algorithm Calculation Features

Features concentration range uses concentration data material that will set the maximum value and minimum value in the *Numeric Up Down* thus displaying the maximum and minimum limits the concentration of materials that may be used in accordance with its role in the preparation of pharmaceutical suspensions.

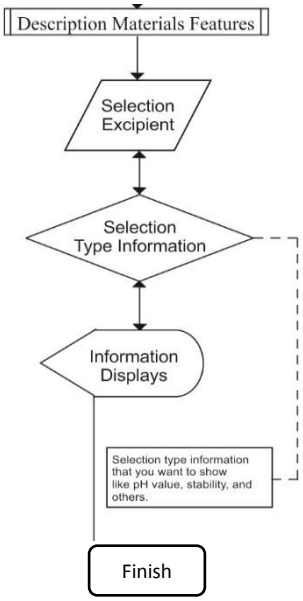


Figure 3. Algorithm Description Materials Features

Features description of materials containing information about physical and chemical properties of additives. This information is taken from the e-book Handbook of Pharmaceutical excipients 5th edition and 6th edition as well as the Indonesian Pharmacopoeia 3th edition and 4th edition.

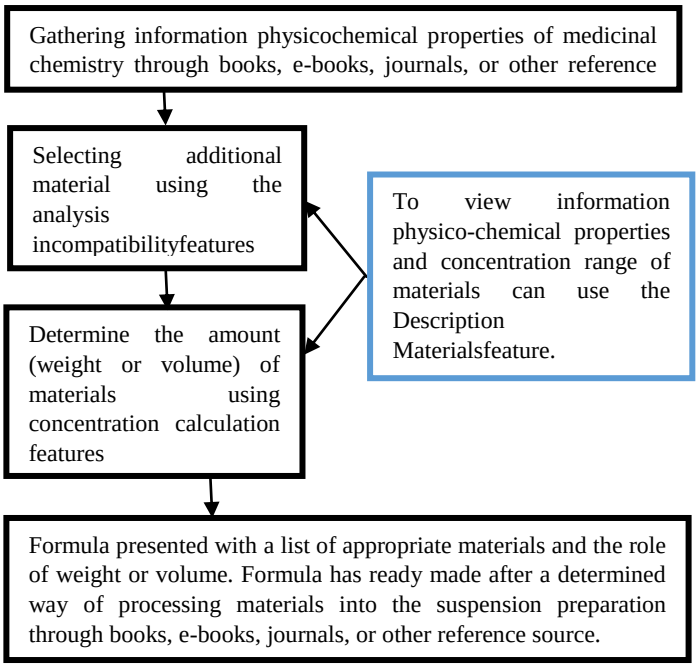
Evaluation Software EXC-Sol

Evaluation is done by looking at aspects of the variable quality of the software described by McCall (1966), but there are some aspects that were not tested because it is not included in the scope of software usability EXC-Sol, besides the evaluation was only strengthened in the simulation material selection. Here is a table of variable quality software EXC-Sol.

Table 1. Variable Software Quality

Variables	Indicator
Reliability (ability of the software can carry out its function)	Test additional material selection by designing 35 formula in accordance with the number of types of materials suspending listed in the Handbook of Pharmaceutical excipients 6th edition
Efficiency (The computing resources required by the software to perform its function)	The accuracy of the order form and button access to the command by pressing each button access to the command and see the suitability of orders carried out by software EXC-Sol.

Pre-formulation of preparations suspension with Software EXC-Sol



3. Result and Discussion

Making Software EXC-Sol

EXC-Sol software built using Microsoft Visual Studio with the programming language BASIC. Programming languages are the commands understood by the computer to perform certain tasks. Visual Basic programming language developed by Microsoft since 1991 is the development of its predecessor the programming language BASIC (Beginner's All-purpose Symbolic Instruction Code) that was developed in the 1950s. Visual Basic is one of the Development Tool are tools to create a wide variety of computer programs, especially those that use the Windows operating system. Visual Basic is a computer programmming language that supports object

(Object Oriented Programming = OOP) (Octovhiana, 2003).

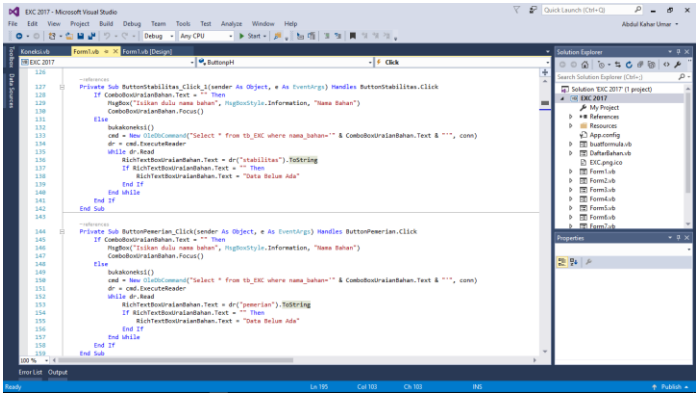


Figure 4. Display coding by following the algorithm design.

In the process of coding, made in accordance with design features except the feature calculation algorithms. In the design of the algorithm, calculate the concentration of the material portrayed in a way that is choosing the material first, and then determine the function or role can be known only after that concentration. But the calculation features are not created as such but included tables Numeric Up Down that play a role in displaying the concentration range of materials automatically where the material has been previously in the analysis features incompatibility.

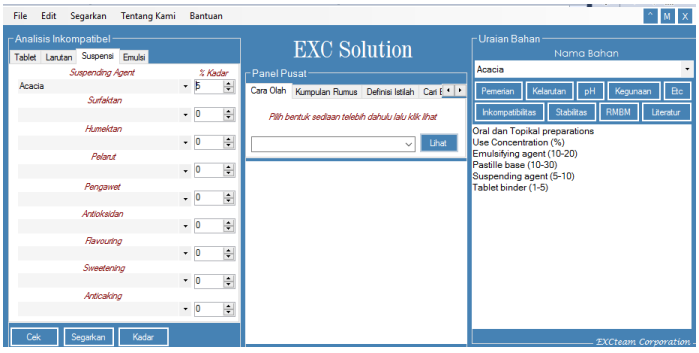


Figure 5. NumericUpDown that displays the concentration of acacia as suspending materials and features material descriptions that displays information on acaciauses.

Table NumericUpDown also has a button to raise or lower the amount of material you want to use concentrations up to the limit of the maximum or minimum concentration where the concentration is maximum and the minimum has been set automatically depending on the concentration range of each ingredient that is no longer required calculation process. In making the EXC-Sol only calculation features are not adapted to the design of algorithms.

Making Database

EXC-Sol software uses databases created by using Microsoft Access. Making the database with Microsoft Access is very easy and also very good for the database to be used offline.

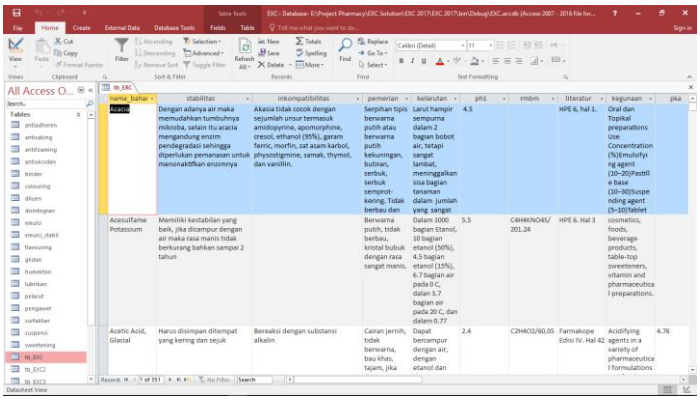


Figure 6. Database created using Microsoft Access.

EXC-Sol in the database, there are two core tables named tb_EXC and tb_EXC8. Tb_EXC used as a container for information data physicochemical properties of the additive while tb_EXC8 used to store data incompatibility additional material. In other words, tb_EXC reserved the description of materials which feature information data physicochemical properties of existing additives in tb_EXC can be accessed via the button-buttonthat exist on the material description features. Data published in the form of names tb_EXC8 material that made the list of ingredients incompatible with it so that the selection of materials using the analysis features incompatibility would read the ingredients are mutually incompatible.

In addition to these two core table, there were also 19 other secondary table that is destined to accommodate the data concentration range of materials according to the role or function.

Evaluation Software EXC-Sol

At this stage, made a total of 35 suspensions formula where output is a notepad file as shown below.

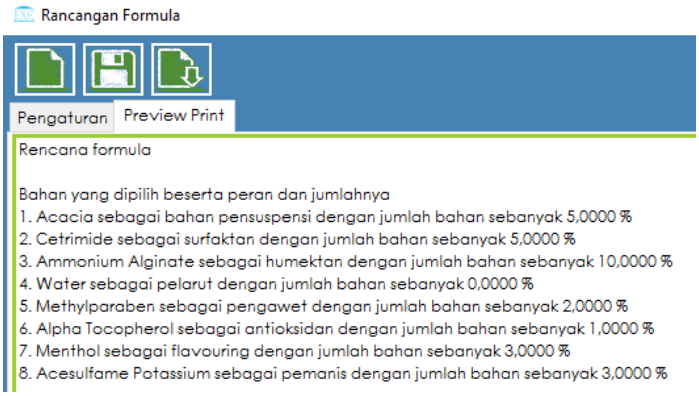


Figure 7. Sample analytical incompatibility results EXC-Solformula

To know that the results of the analysis features of incompatibility are valid then do a comparison of the output data of each ingredient suspending incompatibility with each other supplemental materials from the e-book edition of the handbook of pharmaceutical excipients 6th edition.

In formula 1, according to Raymond (2009) Data incompatibility of each ingredient are outlined as follows. Acacia as a suspending agent incompatible with some substance like amidopyrine, apomorphine, cresol, ethanol (95%), ferric salts, morphine, phenol, physostigmine, tannins, thymol and vanillin. Cetrimide as surfactants incompatible with soap, anionic surfactant, nonionic surfactant with a high concentration, bentonite, iodine, phenylmercuric nitrate, alkali hydroxide and acid colorant. Cetrimide in solution can react with metal ions. Ammonium Alginate as a humectant incompatible with oxidizing agents and acids and strong bases. Methylparaben as a preservative antimicrobial activities will be reduced if there is a nonionic surfactant, such as polysorbate 80, as a result of micelation. However, propylene glycol (10%) has been shown to strengthen the paraben class of antimicrobial activity despite a nonionic surfactant and prevent interaction between methylparaben and polysorbate 80. methylparaben also incompatible with other materials, such as bentonite, magnesium trisilicate, essential oils, sorbitol, talc, tragacanth, and atropine. React with various sugars including sugar alcohols. Methylparaben absorption by plastic have also been reported; the amount absorbed depends on the type of plastic. It has been claimed that polyethylene bottles with low density and high density does not absorb methylparaben. Methylparaben change color if there is iron and hydrolyzed by weak base and a strong acid. Alpha Tocopherol as an antioxidant incompatible with peroxide, metal ions, especially iron, copper, and silver. Menthol as a flavoring incompatible with butylchloral hydrate, camphor, chloralhydrate, chromium trioxide, b-naphthol, phenol, potassium permanganate, Pyrogallol, resorcinol, and thymol. While the sweetener acesulfame potassium as there is no data of its incompatibility.

A comparison between the output of software EXC-Sol on the analysis incompatibility features with the incompatibility data of the handbook of pharmaceutical excipeint 6th edition, it can be seen that the results of the analysis in the first formula with ingredients suspending acacia in Figure 7 in accordance with her incompatibility data where additives such as cetrimide, ammonium alginate, methylparaben, alpha tocopherol, fructose, acesulfame potassium and water as a solvent is not included in the list of ingredients that is incompatible with acacia. Similarly, in other additives have no information that indicates incompatibility with each other.

In evaluating the suitability of keys with a command not found error. Each command button runs well.

4. Conclusion

Based on the research that has been done, it can be concluded that:

1) Designing software algorithms EXC-Sol has been in accordance with the output of the software in the form of a list of additional materials along with the functions and levels.
2) The test result reliability by designing the 35 formula suspensions have been in accordance with the comparison of data incompatibility in the Handbook of Pharmaceutical excipients 6th edition, so it can be stated that the EXC-Solanalysis

results are valid. Similarly, in testing efficiency by looking at the suitability of a button and the mode command can be expressed is appropriate.

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