

Selection of excipient and suitable method for the preparation of nanoparticles containing cyclophosphamide by hierarchy process

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Received: 10th June 2016, Revised and Accepted: 14th June 2016

ABSTRACT

In our present study, an approach has been made to select the polymer and method of preparation of nanoparticles containing Cyclophosphamide. With the wide range of methods and materials available for the manufacturing of nanoparticles, it is very vital for the researcher to select the appropriate method. However, the time and material resources spend in selection of method and materials will curb the prolonged researching time and unnecessary expenditure on trying out at all the method. In our present study an initiative has been taken to tackle the aforementioned issue and to select the appropriate method and polymer by Hierarchy model introduced by Dr. Thomas L Saaty in 1960's. We found that nanoprecipitation method and gumghatti has got the highest priority weights as compared with the rest of the methods and materials respectively.

Keywords: Polymer, Method of nanoparticles, Priority points, Thomas L saaty.

1. INTRODUCTION

Choosing the right coating materials in the formulation of polymer coated capsule dosage form is a crucial decision and so will be the method of nanoparticles preparation. Implementing appropriate evaluation and decision tool should be considered at the selection of coating materials involves many complex decision-making tasks. One of the useful tools that can be employed at the coating material selection is Analytical Hierarchy Process (AHP). The AHP, developed at the Wharton School of Business by Saaty, is a powerful and flexible weighted scoring decision making process to help people set priorities and make the best decision [1]. AHP has been widely used to solve multi-criteria decision making in both academic research and in industrial practice. AHP has been implemented in almost all applications related to decision-making and is currently predominantly used in the theme of selection and evaluation especially in the area of engineering, personal and social categories. Generally, implementing AHP is based on experience and knowledge of the experts or users to determine the factors affecting the decision process. AHP is an intuitive method for formulating and analyzing decisions whereas cited that AHP approach is a subjective methodology.

AHP is not only used as a stand-alone tool but also can be integrated with other techniques. AHP can be combined with other techniques such as quality function deployment (QFD), data envelopment analysis (DEA), and its integration can be employed to a wide variety of fields especially in logistic and manufacturing areas. [2,3]

There are a number of activities in coating material selection process related to decision-making. Various methods have been developed to assist designers to make the right decision at the coating material selection stage in the literature. The simple decision method is the Pugh concept selection method, this method involves qualitative comparison of each alternative to a reference or datum alternative, criterion by criterion. It is useful in coating material selection because it requires the least amount of detailed information. However, no measure is given of the importance of each of the criteria and it does not allow for coupled decisions. Therefore, there is a danger that the final concept can be imprecise. In order to support the efficiency in selecting the coating materials, an appropriate evaluation and decision tools need to be considered [4-8]. Since, AHP application is related to evaluating and selecting different alternatives or options, it can also be implemented in coating material selection process

especially in selecting the most appropriate coating materials. At this stage, designers have to consider a number of factors in order to determine and select the optimum decision options.

It is because the inappropriate decision can lead to possible product to be redesigned or remanufactured. The advantages of using AHP include achieving higher quality product and shorter product development process.

AHP helps capture both subjective and objective evaluation measures, providing a useful mechanism for checking the consistency of the evaluation measures and alternatives suggested by the team thus reducing bias in decision-making. AHP allows organizations to minimize common pitfalls of decision-making process, such as lack of focus, planning, participation or ownership, which ultimately are costly distractions that can prevent teams from making the right choice.

This study discusses AHP implementation in the area of coating material selection process in the development of a polymer coated capsule dosage form. Thus, employing AHP can make the job of coating material selection process shorter, reduce cost and produce higher product quality. Despite some works have been carried out in terms of AHP implementation in coating material selection process, there is still a very limited information or study on the coating material selection in the development of polymer coated capsule dosage form [9,10]. Thus, the study illustrates the use of AHP in evaluating and determining the most suitable coating materials in the development of polymer coated capsule dosage form.

1.1. Analytical hierarchy process principles

Once a hierarchy framework is constructed, users are requested to set up a pair wise comparison matrix at each hierarchy and compare each other by using a scale pair wise comparison¹¹ as shown in table 1.

Finally, in the synthesis of priority stage, each comparison matrix is then solved by an eigenvector method to determine the criteria importance and alternative performance. These principles can be elaborated by structuring them in a more encompassing nine steps process as shown in figure 1.

1.2. Advantages of using AHP

The advantages of using the AHP is as follows Harker and Vargas 1987.

- It formalizes and renders systematic what is largely a subjective decision process

and as a result facilitates “accurate” judgements;

- As a by-product of the method, decision makers receive information about the implicit weights that are placed on the evaluation criteria and
- The use of computers makes it possible to conduct sensitivity analysis on the results.

Table - 1: The 9 point scale for pairwise comparisons

Definition	Explanation
Equal importance	Two elements contribute identically to the objective
Weak dominance	Experience or judgement slightly favours one element over another
Strong dominance	Experience or judgement strongly favours one element over another
Demonstrated dominance	An element’s dominance is demonstrated in practice
Absolute dominance	The evidence favouring an element over another is affirmed to the highest possible order
Intermediate values	Further subdivision or compromise is needed

Another advantage of using AHP is that it results in better communication, leading to a clearer understanding and consensus among members of decision-making groups so that they are likely to become more committed to the alternatives selected [Schoemaker and Waid 1987] AHP also has the ability to identify and take into consideration the decision maker’s personal inconsistencies. Decision makers are rarely consistent in their judgements with respect to qualitative aspects. The AHP method incorporates such inconsistencies into the model and provides the decision maker with a measure of these inconsistencies.

A consistency ratio is taken as the ratio of the consistency of the results being tested to the consistency of the same problem evaluated with random numbers. This ratio provides the user with a value that can be used to judge the relative quality of the results. If a consistency ratio of less than 0.10 is obtained, then the results are sufficiently accurate, and further evaluation is not needed. However, if the consistency ratio is greater than 0.10, the results may be arbitrary and the preferences should be re-evaluated or discarded.

The great advantage of the AHP lies in its ability to handle complex real life problems and with its ease of use. Compared with five different utility models for determining weights and priorities, AHP was found to produce the most credible results of all the models tested.

The ability of the AHP to analyse different decision factors without the need for a common numerate, other than the decision makers' assessments, makes it one of the favourable multicriteria decision support tools when dealing with complex socioeconomic problems in developing countries [12,13]. This is because it enables social, cultural, and other non-economic considerations to be incorporated into the decision-making process.

We illustrate the procedure with the following research study from selecting the best coating material in the preparation of novel capsule.

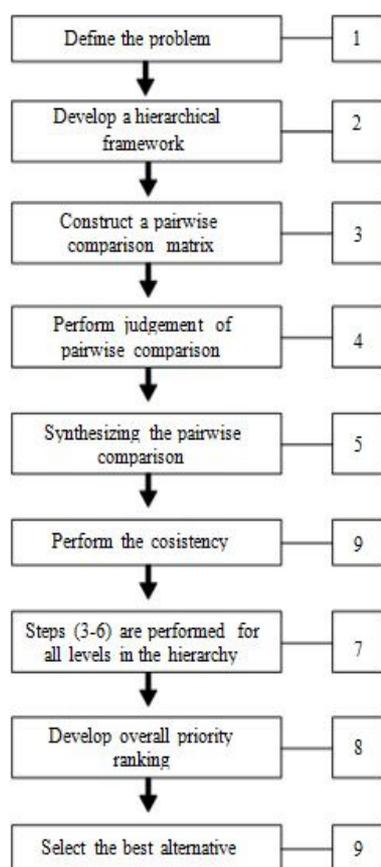


Figure - 1: Sequence of Hierarchy model

2. MATERIALS AND METHODS

For the selection of nanoparticles preparation method and polymer which plays a crucial role in the formulation of nanoparticles, the following criterias are considered with the options as methods and various polymers respectively.

Table - 1: Criteria for the nanoparticles preparation

Criteria	Abbreviation/Code
Availability of instruments	MCR01
Operational tediousness	MCR02
Results reproducibility	MCR03
Process simplicity	MCR04
Economical	MCR05

Table - 2: Options for the preparation of nanoparticles

Options	Abbreviation/Code
Ionic gelation method	SCR01
Nano spray drying method	SCR02
Nanoprecipitation technique	SCR03
Dialysis method	SCR04
Super critical fluid method	SCR05

Table - 3: Criteria for the polymer selection

Criteria	Abbreviation/Code
Dependability	CRT01
Physio-chemical nature	CRT02
Price of material	CRT03
Availability of material	CRT04

Table - 4: Polymer options for selection

Options	Abbreviation/Code
Chitosan	PLR01
Gum Ghatti	PLR02
Eudragit polymers	PLR03

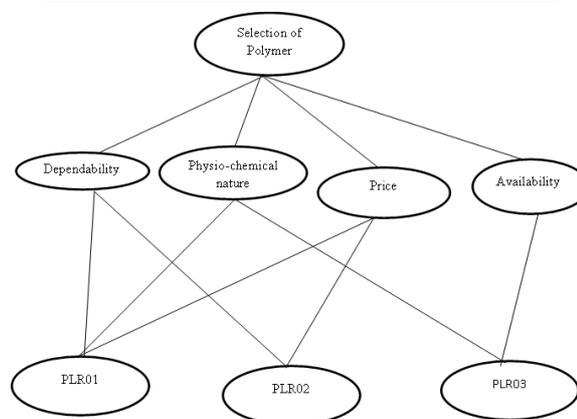


Figure - 2: Hierarchy of Polymer materials selection problem.

3. RESULTS AND DISCUSSION

Generally, AHP consists of three main principles, including hierarchy framework, priority analysis and consistency verification. Formulating the decision problem in the form of the hierarchy framework is the first step of AHP,

with the top level representing overall objectives or goal, the middle levels representing criteria and sub-criteria, and the decision alternatives at the lowest level. The pair wise comparison of all the selected criteria's on each sub criteria's were given in the table 5 - 10.

Table - 5: Criteria with respect to Goal (Selection of excipient and suitable method for nanoparticle preparation)

	MCR01	MCR02	MCR03	MCR04	MCR05	Eigen Vector	Weight	Comp Eigen Vector
MCR01	1	1/2	1/2	3	4	1.2457	0.207	1.0659
MCR02	2	1	4	5	1/2	1.8206	0.3026	2.5461
MCR03	2	1/4	1	9	7	1.9937	0.3313	2.1235
MCR04	1/3	1/5	1/9	1	8	0.5682	0.0944	0.7783
MCR05	1/4	2	1/7	1/8	1	0.3892	0.0647	0.7808

Table - 6: Options with respect to Availability of instruments

	SCR01	SCR02	SCR03	SCR04	SCR05	Eigen Vector	Weight	Comp Eigen Vector
SCR01	1	4	1	1	2	1.5157	0.2625	1.8028
SCR02	1/4	1	4	2	3	1.431	0.2479	1.9348
SCR03	1	1/4	1	9	6	1.6829	0.2915	2.2216
SCR04	1	1/2	1/9	1	6	0.8027	0.139	0.9124
SCR05	1/2	1/3	1/6	1/6	1	0.3413	0.0591	0.3447

Table - 7: Options with respect to Operational tediousness

	SCR01	SCR02	SCR03	SCR04	SCR05	Eigen Vector	Weight	Comp Eigen Vector
SCR01	1	4	4	1	1/3	1.3976	0.2474	2.5949
SCR02	1/4	1	4	4	4	1.7411	0.3082	2.148
SCR03	1/4	1/4	1	8	9	1.351	0.2392	2.0916
SCR04	1	1/4	1/8	1	8	0.7579	0.1342	1.0574
SCR05	3	1/4	1/9	1/8	1	0.4014	0.0711	0.9337

Table - 8: Options with respect to Results reproducibility

	SCR01	SCR02	SCR03	SCR04	SCR05	Eigen Vector	Weight	Comp Eigen Vector
SCR01	1	3	3	3	1/4	1.4651	0.2606	2.3023
SCR02	1/3	1	1	1/3	8	0.9767	0.1737	1.137
SCR03	1/3	1	1	4	9	1.6437	0.2923	1.9684
SCR04	1/3	3	1/4	1	9	1.1761	0.2092	1.4689
SCR05	4	1/8	1/9	1/9	1	0.3615	0.0643	1.1841

Table - 9: Options with respect to Process simplicity

	SCR01	SCR02	SCR03	SCR04	SCR05	Eigen Vector	Weight	Comp Eigen Vector
SCR01	1	4	1	2	2	1.7411	0.2911	1.9566
SCR02	1/4	1	4	3	3	1.5518	0.2595	1.9518
SCR03	1	1/4	1	5	9	1.6227	0.2713	1.7166
SCR04	1/2	1/3	1/5	1	8	0.7677	0.1284	0.8123
SCR05	1/2	1/3	1/9	1/8	1	0.2971	0.0497	0.3279

Table - 10: Options with respect to Economical

	SCR01	SCR02	SCR03	SCR04	SCR05	Eigen Vector	Weight	Comp Eigen Vector
SCR01	1	5	1/2	4	4	2.0913	0.3375	2.1564
SCR02	1/5	1	5	4	1	1.3195	0.2129	2.2247
SCR03	2	1/5	1	6	9	1.8488	0.2983	2.0761
SCR04	1/4	1/4	1/6	1	9	0.6229	0.1005	0.745
SCR05	1/4	1	1/9	1/9	1	0.3147	0.0508	0.3924

The final priority of the listed nanoparticle preparation method has been given in the table 11.

Table - 11: Final Priority for Nanopreparation method

Preparation method	Priority
Ionic gelation method	0.2649
Nano spray drying method	0.2404
Nanoprecipitation technique	0.2745
Dialysis method	0.1573
Super critical fluid method	0.063

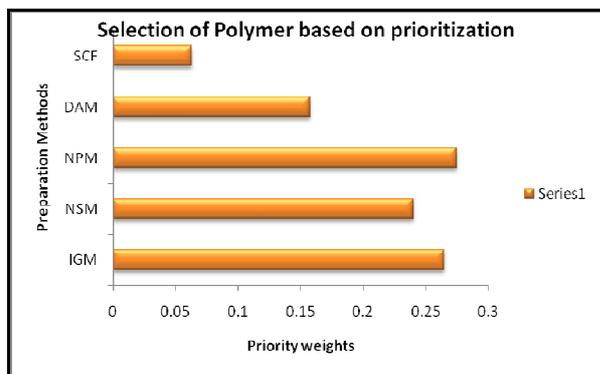


Figure - 3: Selection of nanoparticle preparation method.

The final priority of the list of polymers has been given in the table 12.

Table - 12: Final Priority for polymers

Preparation method	Priority
Chitosan	0.3636
Gum ghatti	0.5182
Eudragit polymer	0.1182

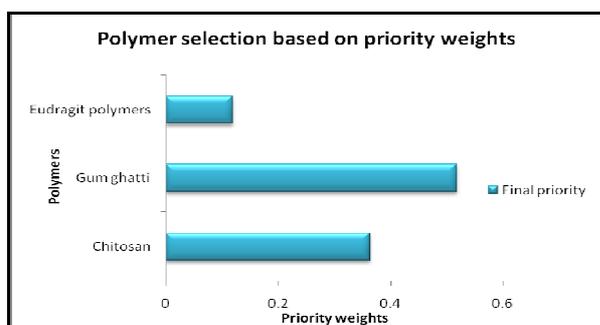


Figure - 4: Selection of polymer.

4. CONCLUSION

We conclude that the, pair wise comparison of the essential parameters (Criteria's) concerned with the priority weights of nanoparticulate preparation method and polymer selection by Hierarchy model has been conducive. Nano precipitation method and gum ghatti polymer has got highest priority weights in the pair wise comparison method using Hierarchy model by Thomas saaty L of lending priorities. Obviously, the nano precipitation method and gum ghatti are the more suitable method for the designing of nanoparticles containing cyclophosphamide. Besides, the utilization of Hierarchy Process for the selection of nanoparticle preparation method and polymer for the designing of Cyclophosphamide has been very useful for our research work to take it to next stage.

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