

**Review Article****Optimisation techniques: a futuristic approach for formulating and processing of pharmaceuticals****REHA S. CHODANKAR*, ASISH DEV***Department of Pharmaceutics, Oriental College of Pharmacy, Sanpada, Navi Mumbai, India.***ARTICLE INFO:****Article history:**

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ABSTRACT

Designing and formulating an ideal pharmaceutical product is a very tedious job for a formulator as it comprises of multiple objectives. The traditional method followed for years is not only expensive and time consuming but it also needs lot of effort to be put in and in spite of that at times it proves to be unfavourable and unpredictable too. The recent approach to optimise i.e. to achieve the best combination of product and process characteristics under the given conditions is by using Design of Experiment (DoE). Design of Experiment (DoE) is an organised approach to determine the relationship between the factors (Xs) affecting a process and the output of that process (Ys). The recent optimisation methodologies include various approaches that come under the 2 main categories namely, simultaneous optimisation and sequential optimisation. Nowadays there are various software available to carry out the optimisation of pharmaceutical products.

Introduction

Earlier, pharmaceutical products were formulated by trial and error method. Whereas formulators knowledge and experience played a vital role in formulation of new dosage forms or modification of existing. At times when skill, wisdom and luck wouldn't favour it would result in waste of energy, time and resources [1]. The traditional way of designing a new formulation involved studying the influence of composition and process variables on dosage form characteristics, changing one single/separate factor at a time (COST), while keeping others constant. The technique is also referred to as changing One Variable at a Time (OVAT) or One Factor at a Time (OFAT). Using this approach the solution to the problem may be achieved but it does not guarantee the true optimum concentration or process. The product obtained may be sub-optimal, as a better formulation may still exist for the studied conditions. Therefore this approach faced various limitations and hence came the modern optimisation technique, which involves systematic design of experiments (DoE) [2].

Limitations of traditional approach include [3]:

- Time consuming
- Energy utilising
- Uneconomical

- Unpredictable
- Unsuitable to plug errors
- Ill-suited to reveal interactions
- Yielding only workable solutions.

Optimisation is the process of finding the best way of using the existing resources while taking into account all the factors that influence decisions in any experiment. It allows finding of the best possible value dependant variable by changing certain independent variables.

The objectives of optimisation involved to maintain the quality, reduce manufacturing costs, and safety of public and industry. Whereas the significance of optimising a pharmaceutical product involved the discovery of important variables involved, cheaper and efficient way of formulating the product and improving the consistency and usefulness of quality specification in the formulation[4].

Design of Experiments

It is an organised method used to determine the relationship between the factors (Xs) affecting a process and the output of that process (Ys). Statistical DoE refers to the process of

planning the experiment in such a way that suitable data can be collected and analysed statistically, resulting in a valid and objective conclusion. This approach is used to draw meaningful conclusions from experimental data [4].

Advantages of DoE [2]

- Requires less number of experiments to achieve an optimum formulation.
- Yields the best solution in the presence of other competing objectives.
- It helps in tracing and rectifying the problem in a remarkably easier manner.
- Lead to complete understanding of the formulation system.
- Helps in finding the important and unimportant input variables.
- Tests and enhances robustness of the experimental studies.
- It allows change of formulation ingredients or processes independently.
- Aids in determining experimental error.
- Can simulate the product or process behaviour using model equation(s).
- Save a significant amount of resources viz. effort, time, materials and cost.
- Evaluate and improve the statistical significance of the proposed model(s).
- It predicts the performance of formulations without preparing them.
- It estimates and detects the possible interactions and additive effects among the variables.
- Facilitates decision making by response mapping before next experimentation.
- Provides reasonable flexibility in experimentation to assess the product system.
- Furnish ample information on formula behaviour from one simultaneous study.
- It decouples signal from background noise which enables inherent error estimation.

Applications of DoE [1, 5]

- Dissolution testing
- Granulation
- Tablet formulation
- Coating of tablets
- Extrusion- Spheronisation (macro particulate dosage forms)
- Transdermal drug delivery system
- Microcapsule / Nanoparticle / Liposome formation (micro particulate dosage forms)
- Fast release dosage forms
- Oral controlled release formulations
- Non oral semisolid
- Miscellaneous formulations

Important terms used in DoE optimisation techniques [1, 5, 8]:

- **Variables** - These are the measurements, values, which are characteristics of the data.
 - **Independent variables:** The input variables, which are directly under the control of the formulator.
 - **Dependant variables:** These are the responses or the characteristics of the resulting products.
- **Factor** - It is an assigned variable e.g. concentration, temperature, emulsifier, gelling agent, and drug: polymer ratio, etc.
- **Levels** - These are the values assigned to the factors. They are indicated as low, middle and high.
- **Response** - It is the effect evaluated from the selected factors and assigned levels.
- **Constraints** – Restrictions set on the levels of a factor.
- **Effect** – Change observed in the response by varying the levels of a factor.
- **Interaction** – It occurs when the effect is not directly proportional to the change in the factor levels.
- **Orthogonality** – When the estimated effects are caused by the main factor of interest and are independent of interactions.
- **Confounding**- When one cannot assess how much of the observed effect is due to the concerned factor.
- **Main effects**- Factor effects averaged at all factor levels.
- **Factor space** – Dimensional space defined by the coded variables.
- **Response surface** – Graphical depiction of mathematical relationship between independent and dependent variables.

Design of Experiments Plan [1]

The steps involved in design of experiments plan include:

Defining the objective

The optimization objective, i.e., the property of interest is clearly defined (e.g., drug release from a compressed tablet). Selected response variables should be such that they provide maximum information with minimal experimental effort and time.

Choice of appropriate computer interface

The choice of appropriate software is vital. The computer package selected for the purpose should ideally encompass the facilities of executing several experimental designs for screening as well as response surface optimization, generating design matrices and response surfaces, and conducting statistical analysis and graphics for model diagnostic analysis.

Screening of the factors and selection of their levels

The independent variables to be investigated should be quantifiable. These are first screened for the identification of the possible factors. Once selected as factors, these variables are investigated for their effect on the dependent variable. The study is usually carried out at two levels to determine the main effect and the possible interactions.

Then, the levels of each variable are established either from the prior experience or from the pilot studies. Factor level selection should be judicious enough to include the optima in the region of interest.

Selecting the optimization methodology

Based on the choice of independent variables and type of response expected, a suitable statistical method is selected. A choice has to be exercised between the various simultaneous or sequential methodologies available. If no information is available on the type of response, a quadratic model should be preferred.

Generating the design matrix

The experimental runs are conducted as per the chosen experimental design and the data are collected. The number of experimental trials required is dictated by the selected design. To measure the inherent variability, a sufficient number of replicates should also be determined.

Conducting the experimental studies

The pharmaceutical dosage forms are formulated as per the selected design model and its requisite number of experiments and further evaluated for the desired response(s).

Finding the optimum

The experimental data are used for generation of a mathematical model and an optimum formula is determined using search methods and/or mathematical optimization methods. This is usually facilitated with the help of suitable computer software.

Validating the results

The predicted optimal formulations are formulated, responses evaluated and inferences drawn. The results are implemented in the process/product development cycle or subsequent planning.

Methodologies of optimisation [1, 5]

DOE can be classified into two types:

- **Simultaneous Optimisation**
Here the experimentation is done before carrying out optimisation.
- **Sequential optimization**
In this case as the optimisation study proceeds experimentation work continues sequentially.
- **Artificial neural network [6]**
This technique is now outdated and no longer used in the field of pharmaceuticals.

Simultaneous Optimisation

It is a model dependant technique and is generally termed as response surface methodology (RSM). Response surface is an area of space defined within upper and lower limits of the independent variables depicting the relationship of these variables to the measured responses. The designs in simultaneous optimisation are often known as response surface designs [1]. The designs frequently in use are:

- Factorial design and modifications
- Central Composite design and modifications
- Mixture designs
- D-optimal designs
- **Factorial design and modifications**

These are the most frequently used response surface designs. This design allows evaluation of multiple factors simultaneously and they are based upon first-degree mathematical model. They fall in two categories: full and fractional.

Full factorial design [1]

Full fractional designs involve studying the effect of all the factors (n) at various levels (x), including the interactions amongst them, with the total number of experiments as xn .

The simplest fractional design involves study of two factors at two levels, with each level coded suitably. FDs are said to be symmetric, if each factor has same number of levels, and asymmetric, if the number of levels differs for each factor.

When the number of factors is 5 or more, a full factorial design requires a large number of runs and is not very efficient. Plackett-Burman design is usually a preferred choice in case of five or more factors.

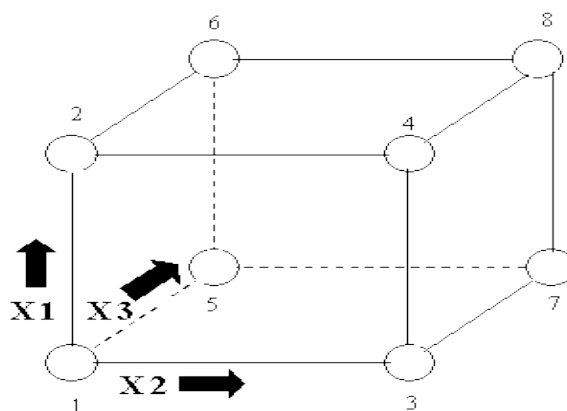


Fig 1: A cube showing 2^3 full factorial design (two level, three factors that implies 8 runs).The numbers indicate the standard order of runs[2]

Fractional factorial design [2]

One difficulty with factorial designs is that the number of combinations increases exponentially with the number of variables that need to be manipulated. Fractional factorial design is used to examine multiple factors effectively with fewer runs than the corresponding full factorial design. It works by assuming that some or all interactions are negligible so that these effects can be confounded with each other.

The types of fractional factorial designs are:

- **Homogenous fractional** - These are used when a large number of factors are to be screened efficiently and higher order interactions are assumed negligible.
- **Mixed level fractional** - These are used for evaluating variety of factors for main effects and higher level interactions are assumed negligible.
- **Box-Hunter** - These are straight forward fractional designs encompassing a wide range of resolutions.
- **Plackett – Burman** - These designs prove to be effective screening designs when only main effects are of interest. They economically detect large main effects, assuming all interactions negligible when compared with few main effects. These designs are also called as saturated designs as it investigates $n*4$ experiments i.e. 8, 12, 16, 20, etc that is suitable for studying up to 7, 11, 15, 19, etc factors respectively.
- **Taguchi** - They allow estimation of main effects while minimising variance and accurate results depend upon absence of any interactions.
- **Latin square** - These are a special case of fractional factorial design wherein there is one factor of interest called treatment factor and two or more blocking (or nuisance) factors. They enable isolation of real effect by counterbalancing the level of the real factor across levels of the nuisance factors.
- **Central composite design and modification [2,7]:**
It is also known as Box-Wilson design; it is the most often used design for second-order models. It contains a factorial or fractional factorial design with centre points that is increased with a group of star points that allows estimation of curvature. If the distance from the centre of the design space to a factorial point is ± 1 unit for each factor, the distance from the centre of the design space to a star point is $|\alpha| > 1$. The precise value of α depends on certain properties desired for the design and on the number of factors involved. Similarly, the number of centre point runs the design is to contain also depends on certain properties required for the design.

Table 1: Types of Central Composite Design [7]

Central Composite Design Type	Description
Circumscribed central composite design	CCC designs are the original form of the central composite design. The star points are placed at some distance α from the centre based on the properties desired for the design and the number of factors in the design. The star points set new extremes for the low and high settings for all factors. Fig. 2 illustrates a CCC design. These designs have spherical, circular, or hyperspherical symmetry and require 5 levels for each factor.
Inscribed central composite design	For those situations in which the limits specified for factor settings are truly limits, CCI design uses the factor settings as the star points and creates a factorial or fractional factorial design within those limits (i.e. a CCI design is a scaled down

CCC design with each factor level of the CCC design divided by α to generate the CCI design). This design also requires five levels of each factor.

Faced central composite design

In this the star points are at the centre of each face of the factorial space, so $\alpha = \pm 1$. This variety requires three levels of each factor.

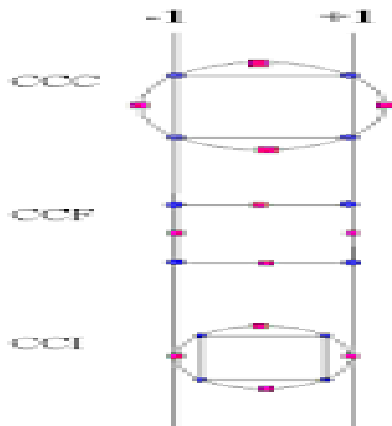


Fig. 2: Illustrates the three types of central composite designs for two factors. Note that the CCC explores the largest process space and the CCI explores the smallest process space. Both the CCC and CCI are rotatable designs, but the CCF is not. In the CCC design, the design points describe a circle circumscribed about the factorial square. For three factors, the CCC design points describe a sphere around the factorial cube.

• Mixture designs [1]:

In pharmaceutical formulations with multiple excipients, the characteristics of the finished product usually do not depend on the quantity of each substance but depends on their proportions. Here, the sum total of the proportions of all excipients is unity and none of the fractions can be negative. Therefore, the levels of the various components can be varied with the restriction that the sum total should not exceed one. In a two-component mixture, only 1 factor level can be independently varied, while in a three-component mixture, only two factor levels can be independently varied. The remaining factor level is chosen to complete the sum to one. Hence, they have often been described as experimental

designs for the formulation optimisation. For process optimisation, designs like Factorial Designs and Central Composite Designs are preferred. There are several types of mixture designs, the most popular being the simplex designs. A simplex is the simplest possible n -sided figure in a $(n-1)$ dimensional space. It is represented as a straight line for two components, as a 2-D triangle for three components, as a 3-D tetrahedron for four components and so on. The design points are uniformly distributed over the factor space and form the lattice. The design point layout for three factors using various models is shown in Fig.3, where each point refers to an individual experiment.

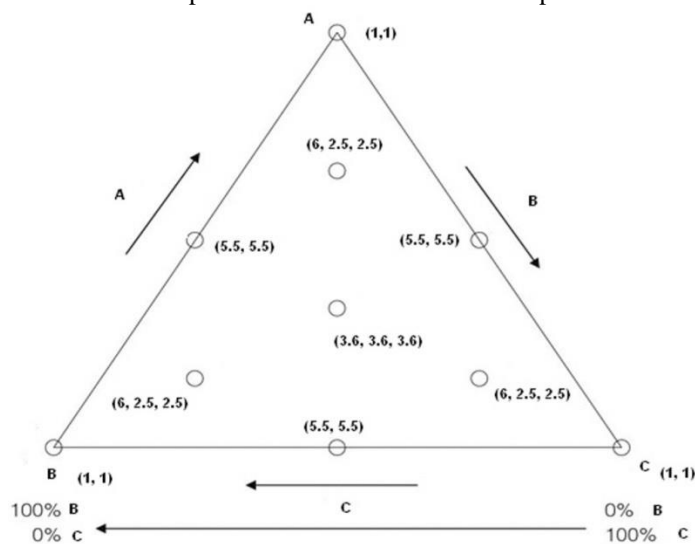


Fig. 3: simplex mixture designs Simplex lattice design for 3 components (A, B and C) system. [21]

- **D-Optimal design [1]**

If the experimental domain is of a definite shape, e.g., cubic or spherical, the standard experimental designs are normally used. However, in case the domain is irregular in shape, D-optimal designs can be used. These are non-classical experimental designs based on the D-optimum criterion, and on the principle of minimization of variance and covariance of parameters. The optimal design method requires that a correct model is postulated, the variable space defined and the number of design points fixed in such a way that will determine the model coefficients with maximum possible efficiency. These designs can be continuous, i.e., more design points can be added to it subsequently, and the experimentation can be carried out in stages. D-optimal designs are also used for screening of factors. Depending upon the problem, these designs can also be used along with factorial, central composite and mixture designs.

➤ **Sequential optimisation[1,5]**

Despite numerous merits of simultaneous approaches, there are situations where there is hardly any prior knowledge about the effects of variables. Such situations call for the application of the sequential methods. In sequential approach, optimization is attempted in a step-wise fashion. Experimentation is started at an arbitrary point in the experimental domain and responses are evaluated. An important aspect of sequential designs is to know when the goal has been accomplished.

Advantages

- No need of planning all the experiments simultaneously,
- Prior knowledge of the response surface not essential,
- Interactive.

Disadvantages

- Number of experiments to reach an optimum cannot be predicted,
- Optimum found may not be the global optimum,
- Robustness is not known,
- Unsuitable for multiple objective problems,
- Attainment of optimum is judged only by the expert developmental scientist,
- Mathematical model and complete response surface is not generated,
- Yields unreliable results when multiple optima exist, and
- Applicable only when response surface is continuous.

The experimental model includes:

- Steepest ascent (descent) methods
- Optimum path method
- Sequential simplex techniques
- Evolutionary operations (EVOP)

- **Steepest ascent (descent) methods:**

This design is a direct optimization method for first-order designs. These approaches are an amalgamation of model-independent and model-dependent methods. The direction of

the steepest increase of the response in terms of coded variables is determined, and then experiments are carried out along this line. This is followed by measurement of the response and is continued until an optimum is reached.

- **Optimum path method**

This method is just analogous to steepest ascent method, where the optimum is also searched outside the experimental domain by extrapolation. Such situations arise when choosing a very extensive experimental domain is difficult or the possible experimental domain is not known at the beginning of the study. However, this method is used for searching the optimum by extrapolation from a second-order design along a curved path.

- **Sequential simplex techniques**

The technique consists of first generating data from $n + 1$ experiments, where n is the number of independent variables or factors. Based on $n + 1$ responses and predetermined rules, one result is eliminated and a new experiment is performed. A decision is made as a result of experimentation, eventually terminating the study at an optimal response.

- **Evolutionary operations (EVOP)**

It is a popular technique in several industrial processes. The underlying basis for this approach is that the production procedure (formulation and process) is continued till the desired results are generated by careful planning and continuous repetition. The process is run in such a way that it produces a product that meets all the specifications and at the same time, generates information on product improvement. Generally, these involve factorial and simplex designs requiring a large number of experiments. In a typical industrial process, this extensive experimentation is usually not a problem, since the process will be run repeatedly over and over again.

➤ **Artificial neural networks[1,6]**

The ANNs are model-independent computational paradigms that can simulate the neurological processing ability of the human brain. ANN is a computer-based learning system that can be applied to quantify a nonlinear relationship between causal factors and pharmaceutical responses by means of iterative training of data obtained from a designed experiment. The results obtained from implementation of an experimental design are used as input information for learning. Once trained, the neurons of an ANN may be used to forecast outputs from new sets of input conditions.

A typical ANN must have one input layer and one output layer, and may contain one or more hidden layers as depicted in Fig. 4. The information is passed from input layer to the output layer through hidden layer(s) by the network connections or synapses. Modelling starts with a random set of synaptic weights and proceeds in iterations. During each iteration, connection weights are adapted via selected modelling. The basis of such modelling technique is to minimize the δ error, i.e., the difference between the

momentary network signal and the aimed signal based on the experimental results. When the minimal " δ error" is obtained, learning is completed and connection weights become the memory units. After this, the test set of values can be applied on a learned ANN to evaluate it. Subsequently, it can be used

for output prediction on the basis of the new input values. The modelling is invariably done via suitable computer software. ANNs require a great deal of iterative computations, the use of versatile computer software dedicated for the purpose becomes almost obligatory for their execution.

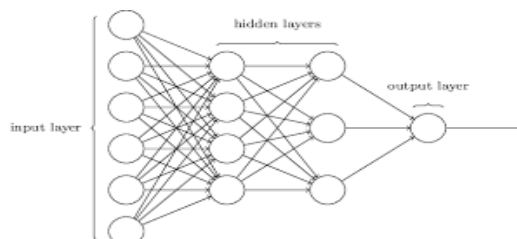


Fig.4: Schematic diagram illustrating various parts of an Artificial Neural Network

Software for optimisation of pharmaceutical product [1, 6] Choice of Computer Software Package

When selecting DoE software, it is important to look for not only a statistical engine that is fast and accurate but also the following:

- A simple graphic user interface (GUI) that's intuitive and easy-to-use.
- A well-written manual with tutorials to get you off to a quick start.
- A wide selection of designs for screening and optimizing processes or product formulations.

- A spreadsheet flexible enough for data entry as well as dealing with missing data and changed factor levels.
- Graphic tools displaying the rotatable 3-D response surfaces, 2-D contour plots, interaction plots and the plots revealing model diagnostics
- Software that randomizes the order of experimental runs. Randomization is crucial because it ensures that "noisy" factors will spread randomly across all control factors.
- Design evaluation tools that will reveal aliases and other potential pitfalls.
- After-sales technical support, online help and training offered by manufacturing vendors

Computer software used for optimisation of pharmaceutical products

Table 2: Different software used in optimisation techniques

Software	Features
Design Expert	optimizing pharmaceutical formulations and processes; allows screening and study of influential variables for FD, FFD, BBD, CCD, PBD and mixture designs; provides 3D plots that can be rotated to visualize the response surfaces and 2D contour maps; numerical and graphical optimization
Mini Tab	Powerful DoE software for automated data analysis, graphic and help features, MS-Excel compatibility, includes almost all designs of RSM
JMP	DoE software for automated data analysis of various designs of RSM, graphic and help features
CARD	Powerful DoE software for automated data analysis, includes graphic and help features
DoE PRO XL & DoE KISS	MS-Excel compatible DoE software for automated data analysis using Taguchi, FD, FFD and PBD. The relatively inexpensive software, DoE KISS is, however, applicable only to single response variable.
MATREX	Excel compatible optimization software with facilities for various experimental designs and Taguchi design.
Cornerstone™	DoE software with features for executing various experimental designs
ECHIP	Used for designing and analyzing optimization experiments
GRG2	Mathematical optimization program to search for the maximum or minimum of a function with or without constraints
DoE PC IV	Used for designing the optimization experiments
STATISTICA	ANN-based software based on GRN technique
NEMROD@	Suitable for FDs and CCDs, has features for numerical optimization and graphic outputs

MODDE	Suitable for response surface modelling and evaluation of fitting of model
SPSS	Comprehensive statistical software with facilities for implementing experimental designs
OMEGA	Only for mixture designs; only program that supports multicriterion decision making by Pareto- optimality, up to six objectives and has various statistical functions
DoE WISDOM	Supports designs for screening, D-optimal, Taguchi and user defined designs, also options are available for pare to optimality charts
COMPACT	Optimization software for systematic DoE and response surface methodology studies with state-of-art mathematical search techniques
OPTIMA	Generates the experimental design, fits a mathematical equations to the data and graphically depicts response surfaces
XSTAT	Aids in selection of an experimental design, has modules for numerical optimization and graphic outcomes
FACTOP	Aids in the optimization of formulation using various FDs, and other designs through development of polynomials and grid search; includes computer-aided-education module for optimization

Table 3: Examples showing the use of optimisation techniques in formulation

Sr No.	Drug	Design	Reference
1	Olmesartan	Full factorial design	Vaddemukkala. Y; 2015.[10]
2	Hyaluronidase	Fractional factorial design	K. Narayanan; 2014. [11]
3	Emtricitabine	Central composite design	Singh G; 2014[12]
4	-	Plackett - Burman design	Jain S; 2010[13]
5	Gliclazide	Taguchi design	J. Varshosaz; 2008[14]
6	Okra tablet as a dietary supplement	D- optimal design	Mohamad Zen; 2015.[15]
7	Ondansetron	Artificial neural network	Buket Aksu; 2014. [16]
8	Tenofovir	Box- Behnken	Kefilwe Matlhola; 2015[17]
9	Prednisolone	Face centred composite design	Saini R; 2012.[18]
10	Levocetirizine Dihydrochloride	Response surface method	Dhiman S; 2011. [19]
11	Glipizide	circumscribed central composite design	Habibuddin M; 2015. [20]

References

- Singh B, Gupta R.K., Ahuja N; Computer assisted optimization of pharmaceutical formulations and processes; January 2006, publication 232746895.
- Singh B, Kumar R, Ahuja N; Optimizing Drug Delivery Systems Using Systematic "Design of Experiments." Part I: Fundamental Aspects; Critical Reviews in Therapeutic Drug Carrier Systems; February 2005.
- Singh, Bandopadhyay S, Kapil R, Ahuja N; systematic Optimisation of Drug Delivery Systems: An Insight. The Pharm Rev.2008; 7 : 146-186.
- Shobha Rani R Hiremath, Vanaja K; Optimisation Techniques in pharmaceutical formulation and processing; Textbook of Industrial Pharmacy: Drug Delivery Systems, and Cosmetic and Herbal Drug Technology; pg no. 158-168.
- Siddheshwar S, Varpe P, Waghmare G, Wadghule P, Vikhe D; Optimisation Techniques: A Future of Pharmaceutical Product Development; International Journal of Current Trends in Pharmaceutical Research; 2014, Vol.2(3): 491-493.
- Ladani R, Patel M, Dr Patel R, Bhatt T.V; Modern Optimisation Techniques in Field of Pharmacy; Research Journal of Pharmaceutical, Biological and Chemical Sciences; 2010; 1 (2): 148.
- Central composite design; <http://www.itl.nist.gov/div898/handbook/pri/section3/pri3361.htm>
- Schwartz J, Merck Sharp & Dohme Research Laboratories; Recieved May 6, 1981; pg no. 287-301.
- Jethara S, Patel M; Optimizing Oral Controlled Release Drug Delivery Systems using Experimental Designs; Intel Prop Rights 2015, 3:1 <http://dx.doi.org/10.4172/2375-4516.1000135>.
- Vaddemukkala Y, Syed M, Srinivasarao; Research Article On Optimization Of Olmesartan Tablet Formulation By 23 Factorial Design; International Journal of Research in Pharmaceutical and Nano Sciences. 4(4), 2015, 188 - 195.
- K. Narayanan, V. M. Subrahmanyam, and Rao V ;A Fractional Factorial Design to Study the Effect of Process Variables on the Preparation of

- Hyaluronidase Loaded PLGA Nanoparticles; Enzyme Research 2014:12
12. Singh G, Pai R; Optimization (Central Composite Design) and Validation of HPLC Method for Investigation of Emtricitabine Loaded Poly(lactic-co-glycolic acid) Nanoparticles: In Vitro Drug Release and In Vivo Pharmacokinetic Studies; Scientific World Journal 2014:12
 13. Jain S, Singh P, Javeer S, Amin P; Use of Placket-Burman Statistical Design to Study Effect of Formulation Variables on the Release of Drug from Hot Melt Sustained Release Extrudates; AAPS PharmSciTech, 2010;11(2):10
 14. J. Varshosaz, N. Tavakoli, M. Minayian, N. Rahdari; Applying the Taguchi Design for Optimized Formulation of Sustained Release Gliclazide Chitosan Beads: An In Vitro/In Vivo Study; AAPS PharmSciTech, Vol. 10, No. 1, March 2009 (# 2009) DOI: 10.1208/s12249-009-9191-8
 15. Nur Izzati Mohamad Zen, Siti Salwa Abd Gani, Rosnah Shamsudin, Hamid Reza Fard Masoumi; The Use of D-Optimal Mixture Design in Optimizing Development of Okara Tablet Formulation as a Dietary Supplement; e Scientific World Journal 2015:13
 16. Buket Aksu, Gizem Yegen, Sevim Purisa, Erdal Cevher and Yıldız Özsoy; Optimisation of Ondansetron Orally Disintegrating Tablets Using Artificial Neural Networks; Tropical Journal of Pharmaceutical Research September 2014; 13 (9): 1374-1383.
 17. Kefilwe Matlhola, Lebogang Katata-Seru, Lesego Tshweu, Indra Bahadur, Gertrude Makgatho, and Mohammed Balogun; Formulation and Optimization of Eudragit RS PO-Tenofovir Nanocarriers Using Box-Behnken Experimental Design; Hindawi Publishing Corporation Journal of Nanomaterials 2015:12
 18. Saini R, Saini S; Formulation And Optimization Of Osmotically Controlled, Microbially Triggered Colon Targeted System Using Face Centred Central Composite Design; IJPSR (2012), Vol. 3, Issue 09.
 19. Dhiman S, Verma S; Optimization Of Melt-In-Mouth Tablets Of Levocetirizine Dihydrochloride Using Response Surface Methodology; International Journal of Pharmacy and Pharmaceutical Sciences; Received: 12 Feb 2011, Revised and Accepted: 18 May 2011.
 20. Dash R N, Habibuddin M, Touseef H, Ramesh D; Design, optimization and evaluation of glipizide solid self-nanoemulsifying drug delivery for enhanced solubility and dissolution; Saudi Pharmaceutical Journal (2015) 23, 528–540.
 21. Jayaramu R.A, Boregowda S, Varma R, Kalegowda C; Development of fast dispersing tablets of neбиволол: experimental and computational approaches to study formulation characteristics; Brazilian Journal of Pharmaceutical Sciences.50, 2014;50(4):12

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