International Journal of General Medicine
and Pharmacy (IJGMP)
ISSN(P): 2319-3999; ISSN(E): 2319-4006
Vol. 5, Issue 2, Feb - Mar 2016; 33-38

International Academy of Science,
Engineering and Technology
Connecting Researchers; Nurturing Innovations

A STUDY OF G-OPTIMAL FRACTIONAL FACTORIAL DESIGNS IN PHARMACOLOGICAL RESEARCHES

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ABSTRACT

Optimal designs are specified with the goal of obtaining efficient parameter estimates and maximum power of statistical tests while minimizing cost and effort. Many challenges and complexities arise when trying to understand a system with multiple medical treatments because the underlying biological system is intrinsically complex and there are potential multiple interaction. In such cases, efficient fractional factorial designs are useful to study complexity. In the present investigation, G-optimal fractional factorial designs are studied and showed its applicability to study multiple medical treatments interactions

KEYWORDS: Optimal Designs, Fractional Factorial Designs, Prediction Variance, Blocked Designs, etc

INTRODUCTION

In attempting to assess the contributions of medical care to health improvements, the goals of care must first be addressed. The saving of lives in acute life-threatening emergencies is an important such goal. Pharmacology plays key role to achieve such type of goals. In the past few decades, the value of medicine has been clearly demonstrated by the longer life expectancy, a lower infant mortality rate and the higher quality of life. Pharmacological research involves investigation proposed medical treatments and assessing the relative benefits of competing therapies but also involves establishing optimal treatment combination. In the past years, the different studies shows that statistics is an important tool in pharmacological research that is used to summarize experimental data in terms of variance but more importantly it enables us to construct experimental designs with optimum treatments combinations. This is particular importance when attempting to determine pharmacological effect of combination of treatment. In general, pharmacological experiments should be designed in such a way that maximum information can be obtained from minimum number of runs. When the run size of full fractional factorialdesigns increases rapidly then fraction of full factorial design is used.

Fractional factorial designs enable pharmacologicalresearcher to investigate many factors in an economical numbers of runs. The most commonly used criterion for design selection is the minimum aberration criterion proposed by Fries and Hunter (1980), which includes the maximum resolution criterion Box and Hunter (1960). Characterize minimum aberration blocked designs in terms of their blocked residual designs and gave collection of minimum aberration blocked designs with all 8, 16 runs and 32 runs up to 20 factors develop a theory Chen and Cheng (1999). The study of blocking in fractional factorial designs is complicated by the presence of two defining contrast subgroups, one defining the fraction and second defining the blocking scheme. Therefore defining the combination used two types of word-length patterns, one for treatment and another for block. Cheng and Wu (2002) have initiated four combined sequences to elaborate the minimum aberration criteria. The two-level factorial design that has no partial aliasing must be a design or replicate of a design is a

more general results factorial design [Kenny (2004)]. Chetan et al. (2016) constructthe multi-factor mixture experiments using fractional factorial design as an initial design obtained by the minimumaberration criteria.

METHODOLOGY

In pharmacology, the many situations may arise where the number of runs increases rapidly and it create the complication and expensive in analysis. Then the application of factorial design is used to overcome such type of situation. Lie et al. (2009) study the yield of pepsin soluble collagen from muscle of Clarias fish. The experiment was conducted with 8 treatments each with 2 levels.

Table 1

Treatment	Process Variables	Factor Levels	
		Low (−)	High (+)
A	Acetic acid concentration (m)	0.1	0.9
B	Acid extraction time (hr.)	4	8
C	Acid extraction temperature (c)	5	15
D	Acetic acid to muscle ratio (m/g)	5	20
E	NaoH concentration(m)	0.1	0.9
F	NaoH to muscle ratio (m/g)	5	10
G	NaoH treatment time (hr.)	2	6
H	Exraction stirring speed(rpm)	100	250

2^{8-4} Fractional factorial design for such experiment is given by

Table 2

Run	*A*	*B*	*C*	*D*	*E*	*F*	*G*	*H*
1	0.1	4	5	5	0.1	5	2	100
2	0.9	4	5	5	0.1	10	6	250
3	0.1	8	5	5	0.9	5	6	250
4	0.9	8	5	5	0.9	10	2	100
5	0.1	4	15	5	0.9	10	6	100
6	0.9	4	15	5	0.9	5	2	250
7	0.1	8	15	5	0.1	10	2	250
8	0.9	8	15	5	0.1	5	6	100
9	0.1	4	5	20	0.9	10	2	250
10	0.9	4	5	20	0.9	5	6	100
11	0.1	8	5	20	0.1	10	6	100
12	0.9	8	5	20	0.1	5	2	250
13	0.1	4	15	20	0.1	5	6	250
14	0.9	4	15	20	0.1	10	2	100
15	0.1	8	15	20	0.9	5	2	100
16	0.9	8	15	20	0.9	10	6	250

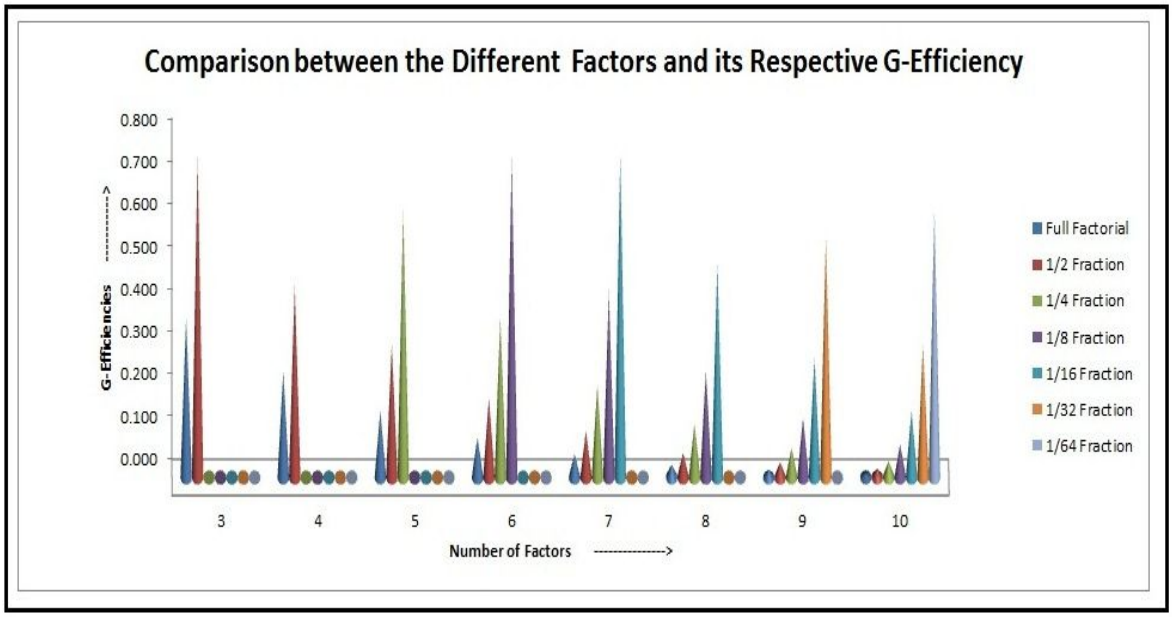
2^{8-4} Fractional factorial design average predicted variance on design space or G-efficiency is 0.562. Its predicted variance is approximate 50 % maximum variance as compare to 1/8 fraction of 2^8 factorial design.Fractional factorial design provides efficient results in terms of number of runs, time, money or information.

To elaborate the concept used the G-efficiency criterion, which indicates to minimize the maximum entry in the diagonal of the hat matrix $x(x'x)x'$. This has the effects of minimizing the maximum variance of predicted values.All the predicted variance related the design space is given in the following table

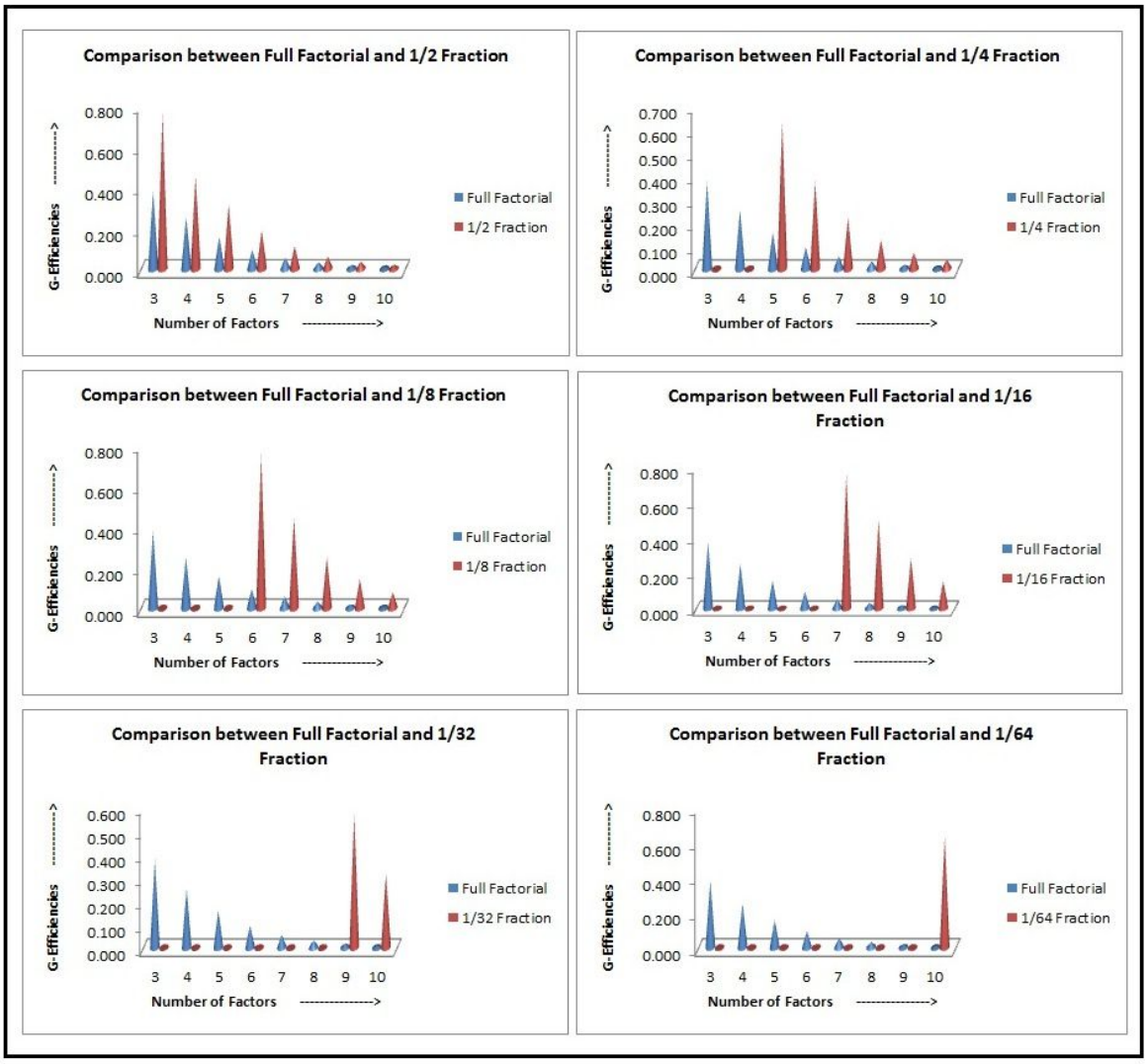
Table 3

Factor	Full Factorial	1/2 Fraction	1/4 Fraction	1/8 Fraction	1/16 Fraction	1/32 Fraction	1/64 Fraction
3	0.375	0.750					
4	0.250	0.450					
5	0.156	0.313	0.625				
6	0.094	0.188	0.375	0.750			
7	0.055	0.109	0.219	0.438	0.755		
8	0.031	0.059	0.125	0.250	0.500		
9	0.018	0.035	0.070	0.141	0.281	0.563	
10	0.010	0.020	0.039	0.078	0.156	0.313	0.625

According to G-efficiency criterion four factors at two-levels, 2^{4-1} fractional factorial design provide the maximum predicted variance on the design space with regard of 2^4 fractional factorial design. Six factor at two level 1/2 fraction of factorial design predicted variance is 0.09375, $1/4$ fraction of factorial design is 0.1875 When fraction increases in the design average prediction variance over design space is increases, so $1/4$ fraction provides near about 50% maximum predicted variance to the previous fraction on design space. But mostly time discard the use of $1/16$ fraction or prefer $1/4$ fraction because 2^{6-4}consider 4 run in the comparison of $2^{6-2}16$ run , 4 run do not describes or explain the true analysis of the design. In case of seven factors at two-level similar pattern are used, when fraction increases every step it affects the predicted variance in the design.



Graph 1: Comparison between Different Factors and its Relative G-Efficiency



Graph 2: Comparison between Full Factorial and Different Fractions

DISCUSSIONS AND CONCLUSIONS

There are many example (having a large number of factors) of use of experimental design for its study in the pharmacology literature. Using a fractional factorial design enable to study four or more factors to be included simultaneously in an experiment of a practicable size, so that the investigator can discover quickly which factors have an important effect on the products. The reduction in the size of the experiments is not obtained without paying a price. The results interpreted in this paper is fractional factorial design provide efficient predicted variance related to design space at the different fraction of the factorial design.

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