Application of Statistical Methods in Pharmacology

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ABSTRACT: In this paper we estimate the number of patients to have a particular type of remedy like no relief, one percent to fifty percent relief, fifty one percent to ninety percent relief and ninety one to hundred percent relief after administering the drug manufactured by a firm for curing a disease so that its curing capacity is on par with drugs produced by other two firms which are known to be best medicine for curing the same disease. These estimations are obtained using the Chi-square goodness of fit and they were shown graphically for various fixed number of patients with no relief and total relief. It helps the firm to decide whether modification of drug is required or not. Further a matlab program is written to give the output "on par with the two medicines" or "not on par with these two medicines" taking the input data of number of patients of each type.

INTRODUCTION:

Statistical methods have been applied in various fields such as pharmaceutical industry, medicine, quality control, biological sciences and economics. Testing of hypothesis is one of the tools in statistical methods. It is can be used in pharmacological research to determine whether the pharmacological effect of one drug is superior to another or equivalent. The use of Statistics in pharmacology was discussed by D.Spina[1] and some examples of the use of statistics in Pharmacology are given by C.V. Winder [2]. The graph (Fig.10) of [3] showing the probabilities of there being n=0are computed for various times is similar to the graph (Fig.2.2) of [4] which is drawn concentration and dosage response curves. The different companies manufacture variety of drugs to cure a disease. If a drug manufactured by a company is not good with respect to curing the disease then the company has to make certain modifications in the medicine to improve the curing capacity of the disease. Researchers in the quality control of pharmaceutical industry have to modify the drug effect by combining it with another drug or add some other substance to the existing composition to improve its curing capacity of the disease. Pharmacoepidemiology is the study of effects of drugs and it is useful to improve the curing capacity of the drug. The medicine with new composition has to be tested with the patients. The present paper helps the researchers to verify the curing capacity of the medicine with other two medicines which are supposed to good in curing the disease. The amount of relief to the patients

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is different from a patient to another because of their resistance power and other conditions or not following the instructions given by doctor. Therefore, we divided the amount of relief as no relief, 1% to 50%, 51% to 90% and 91% to 100% relief. We refer these types of reliefs as type-1, type-2, type-3 and type-4 respectively.

In this paper, we considered the data of two medicines Y and Z produced by two companies in curing the disease and they are supposed to be good in curing the disease. Chi-square goodness of fit given in text Kapoor [5] is used to test whether they have equal effect on curing the disease. The bounds for the number of patients with no relief by the new or modified medicine X are estimated using the Chi-square goodness of fit. Such tests are useful for the researchers who are preparing or modifying the drug to make it on par with medicines Y and Z. We have considered the data of two medicines Y and Z for curing the disease after administering these medicines to hundred patients each. The data contains the number of patients having remedy of type-1, type-2, type-3 and type-4. We take the number of patients with no relief as one parameter and the number of patients with total relief as another parameter. Assigning some particular values to these parameters, we have obtained the possible values of number of patients with other two types of relief so that the new medicine or modified drug will have same effect as that of two medicines Y and Z in curing the disease.

It is observed that if the number of patients of type-1 is 3 and number of patients of type-4 is 20 , we have obtained the possible values of number of patients of type-2 and type-3 are (10, 67),(11, 66),……(31,46) so that the medicine X will have the same curing capacity of the medicines Y and Z. The data collected on experimenting the medicine can be compared with theoretical results and can make a conclusion about its curing capacity as that of other two medicines which are supposed to be good. A matlab program is written to give the output "On par with two medicines" or "Not on par with two medicines" by taking the complete data of number of patients of each type.

MATERIALS:

The following is the data pertaining to the number of patients of type-1, type-2, type-3 and type-4 relief of 100 patients each after the consumption of the Drug Y and Drug Z which are produced by the companies B and C.

% of curing the disease	Drug Y	Drug Z	Total
	Observed	Observed	
No relief	2	7	9
1 % to 50%	16	18	34

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51% to 90%	53	46	99
91 % to 100 %	29	29	58
Total	100	100	200

Methods:

We set up the null hypothesis H_0: The drugs Y and Z have equal effective in curing the disease. The computed expected frequencies are shown in the following table.

	Drug Y		Drug Z		Total
	Observed	Expected	Observed	Expected	Observed
No relief	2	4	7	5	9
1 % to 50%	16	17	18	17	34
51% to 90%	53	50	46	50	99
91 % to 100 %	29	29	29	28	58
Total	100	100	100	100	200

The Chi-square is defined as $\chi^2 = \sum (O_i - E_i)^2 / E_i$ and the calculated Chi-square value is 2.4534. From the Chi-square tables χ^2 tabulated value is 7.815 at 5% level of significance with 3 degrees of freedom. Since $\chi_{cal}^2 < \chi_{tab}^2$, the null hypothesis can't be rejected. Therefore, we conclude that the drugs Y and Z produced by the companies B and C are equally effective in curing the disease.

Suppose if a company A wishes to produce or modify the drug X so that the drug X will have equal capacity of curing the disease as to that of drugs Y and Z then drug manufactured by the company A has to administer the drug to 100 patients and collect the number of patients p ,q, r and s where p is the number of patients of type-1 remedy, q be the number of patients with type-2 remedy, r be the number of patients with type-3 remedy and s be the number of patients with type-4 remedy.

Case (i): Number of patients of p= 3 and s=20

Suppose the numbers of patients with type-1 and type-4 cure are 3 and 20. We wish to know the possible values of q and r so that the medicine X shall have the same curing capacity as that of medicine Y and Z. Table-1 shows the number of patients of type-2 and type-3 Chi square value three attributes. If the values of q and r in a row against the chi square value that is less than tabulated chi square value 12.592 then we can consider the drug is on par with

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the other two medicines. From the statistical tables the χ^2 value for 6 degrees of freedom is 12.592 at five percent level of significance.

For example p=3,q=10, r=67,s=20 medicine X will have same curing capacity as that of medicines Y and Z since χ^2 calculated is less than χ^2 tabulated value . Similarly p=3,q=11, r=66,s=20,….,and p=3,q=24, r=53,s=20(see Fig.1).

Table-1: Table showing q, r and Chi-square values for fixed p=3 and s=20

Number of patients		Chi square value	Number of patients		Chi square value
q	r		q	r	
1	76	28.49359	40	37	22.64359
2	75	26.14014	41	36	24.26137
3	74	23.98784	42	35	26.00359
4	73	21.31781	43	34	27.20455
5	72	19.46626	44	33	29.02797
6	71	17.80364	45	32	30.97378
7	70	15.95192	46	31	32.3125
8	69	14.54121	47	30	34.33834
9	68	13.30907	48	29	36.48476
10	67	12.07389	49	28	37.96978
11	66	11.05571	50	27	40.19597
12	65	10.20723	51	26	42.54121
13	64	9.444979	52	25	44.18416
14	63	8.780627	53	24	46.60972
15	62	8.278312	54	23	49.15304
16	61	7.885469	55	22	50.96859
17	60	7.543627	56	21	53.59359
18	59	7.357167	57	20	56.33526
19	58	7.258547	58	19	58.34119
20	57	7.213675	59	18	61.16667
21	56	7.318376	60	17	64.10794
22	55	7.459276	61	16	66.32528
23	54	7.690442	62	15	69.35324
24	53	8.066087	63	14	72.49633
25	52	8.40692	64	13	74.94957

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26	51	8.896923	65	12	78.18298
27	50	9.526923	66	11	81.53106
28	49	10.03951	67	10	84.24849
29	48	10.7742	68	9	87.6913
30	47	11.64495	69	8	91.24849
31	46	12.30988	70	7	94.26264
32	45	13.27768	71	6	97.91978
33	44	14.37806	72	5	101.6912
34	43	15.18284	73	4	105.0393
35	42	16.37433	74	3	108.9168
36	41	17.69533	75	2	112.9086
37	40	18.63308	76	1	116.6334
38	39	20.04069	77	0	120.7383

If number of patients of type-2 are less than 10 or greater than 31 for fixed number of patients of type-1 and type-4 are 3,20 respectively then the curing capacity of the drug X is not same as that of the drugs Y and Z **(**Fig.1). When r=77-q then that drug X has same curing capacity as that of Y and Z where q=10, 11, 12 ….31 for p=3 and s=20.

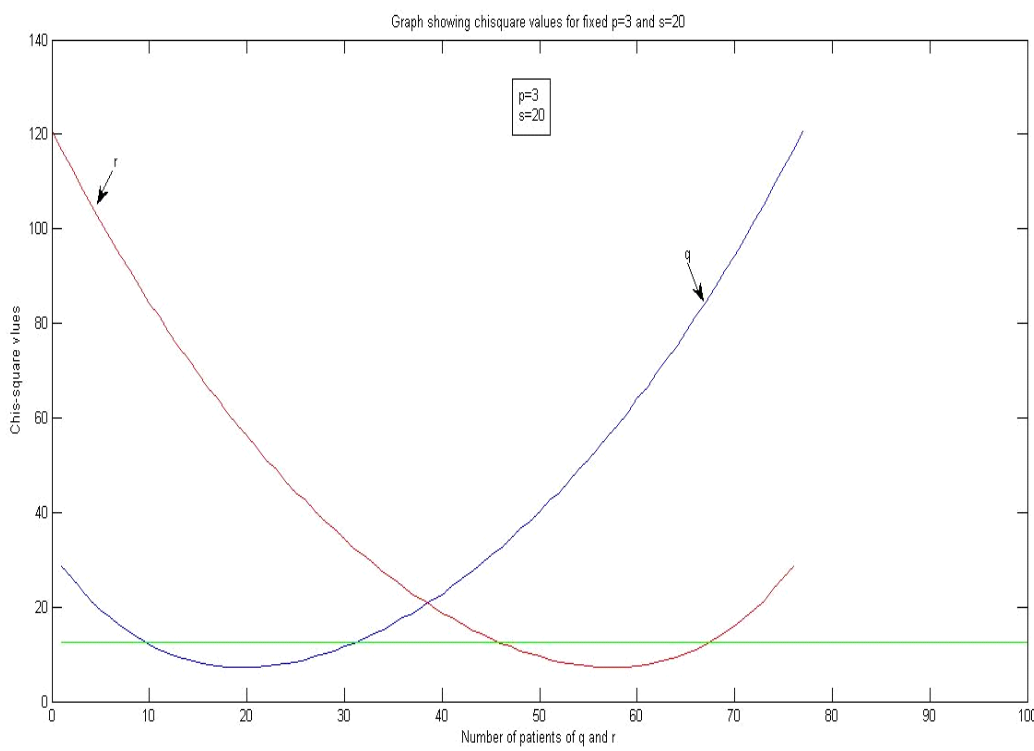

Fig1. Graph showing the chi-square values for fixed values of p=3 and s=20

Case (ii): Number of patients of type-1 and type-4 are 6 and 24

If number of patients of type-2 are less than 6 or gresater than 32 for the fixed number of patients of type-1 and type-4 are 6,24 respectively then the curing capacity of the drug X is not same as that of the drugs Y and Z **(**Fig.2). If r=77-q then the drug X is on par with that of drugs Y and Z where q=6,7,8,9,……,30,31,32 for p=6 and s=24.

Table-2: Table showing q, r and Chi-square values for fixed p=6 and s=24

Number of patients		Chi square value	Number of patients		Chi square value
q	r		q	r	
1	69	22.810582	36	34	18.199392
2	68	20.614153	37	33	19.319781
3	67	18.676599	38	32	20.967508
4	66	16.021238	39	31	22.855017
5	65	14.331728	40	30	24.094746
6	64	12.869801	41	29	25.962653
7	63	11.061905	42	28	28.118201
8	62	9.818519	43	27	29.471754
9	61	8.775991	44	26	31.556003
10	60	7.612	45	25	33.987791
11	59	6.766737	46	24	35.452213
12	58	6.5001	47	23	37.750316
13	57	5.434437	48	22	40.469444
14	56	4.9489	49	21	42.043915
15	55	4.624483	50	20	44.554630
16	54	4.3512	51	19	47.575234
17	53	4.194336	52	18	49.260753
18	52	4.186100	53	17	51.984006
19	51	4.227407	54	16	55.323459
20	50	4.374074	55	15	57.122612
21	49	4.662056	56	14	60.059454
22	48	4.960242	57	13	63.738639
23	47	5.389887	58	12	65.655436
24	46	5.959235	59	11	68.808008
25	45	6.471296	60	10	72.851673
26	44	7.167130	61	9	74.891435

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27	43	8.007289	62	8	78.262963
28	42	8.701160	63	7	82.700165
29	41	9.649488	64	6	84.869456
30	40	10.753646	65	5	88.464262
31	39	11.605519	66	4	93.328917
32	38	12.795242	67	3	95.635512
33	37	14.159933	68	2	99.459041
34	36	15.152335	69	1	104.790592
35	35	16.574557	70	0	107.243482

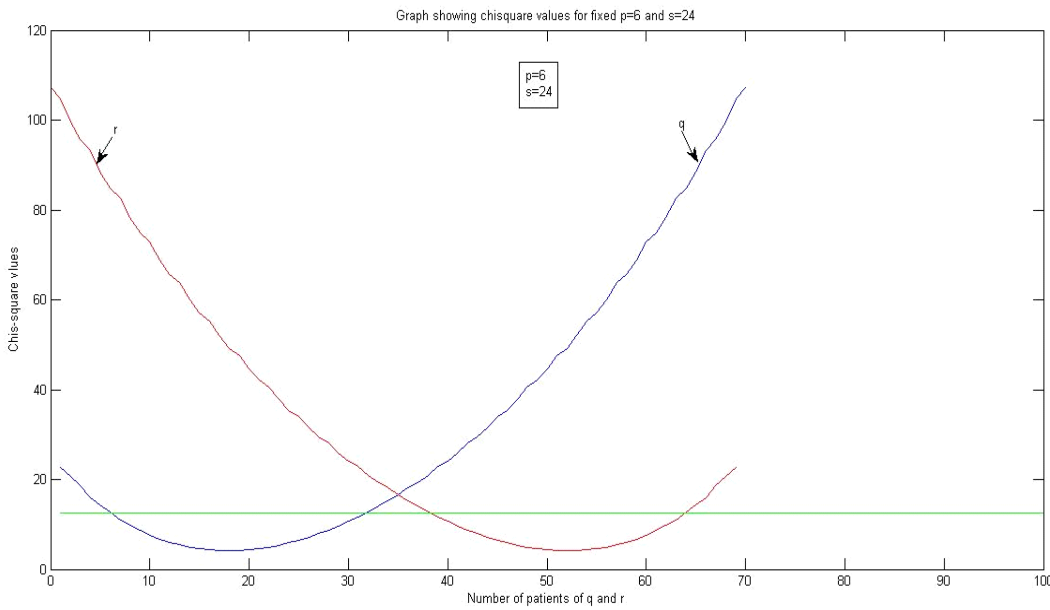

Fig.2 Graph showing chi-square values for fixed values of p=6 and q=24

Case (iii): Number of patients of type-1 and type-4 are 17 and 6

If p=17 and s=6 then the curing capacity of the drug X is not same as that of drug Y and Z for any values of q and r so that q+r =77(Fig.3). We can observe that no value of r and q are below the line parallel to x-axis which represents tabulated Chi-square value. Further **it** is also observed that for any s with p=17 the curing capacity of the drug X is not same as that of other two drugs Y and Z.

Table-3: Table showing q, r and Chi-square values for fixed p=17 and s=6

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Number of patients		Chi square value	Number of patients		Chi square Value
q	r		q	r	
1	76	52.726190	40	37	46.876190
2	75	50.372742	41	36	48.493968
3	74	48.220443	42	35	50.236190
4	73	45.550414	43	34	51.437146
5	72	43.69863	44	33	53.260573
6	71	42.036244	45	32	55.206377
7	70	40.184524	46	31	56.545097
8	69	38.773810	47	30	58.570936
9	68	37.541667	48	29	60.717362
10	67	36.306494	49	28	62.202381
11	66	35.288312	50	27	64.428571
12	65	34.439827	51	26	66.773810
13	64	33.677579	52	25	68.416757
14	63	33.013228	53	24	70.842324
15	62	32.510913	54	23	73.385638
16	61	32.118070	55	22	75.201190
17	60	31.776227	56	21	77.826190
18	59	31.589768	57	20	80.567857
19	58	31.491148	58	19	82.573792
20	57	31.446276	59	18	85.399267
21	56	31.550977	60	17	88.340541
22	55	31.691877	61	16	90.557879
23	54	31.923043	62	15	93.585840
24	53	32.298688	63	14	96.728932
25	52	32.639524	64	13	99.182169
26	51	33.129524	65	12	102.415584
27	50	33.759524	66	11	105.763660
28	49	34.272109	67	10	108.481092
29	48	35.006803	68	9	111.923903
30	47	35.877551	69	8	115.481092
31	46	36.54248	70	7	118.495238
32	45	3.510281	71	6	122.152381
33	44	38.610660	72	5	125.923810
34	43	39.415444	73	4	129.271942
35	42	40.606934	74	3	133.149393

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36	41	41.927933	75	2	137.141223
37	40	42.865683	76	1	140.86603
38	39	44.273292	77	0	144.970867
39	38	45.807712			

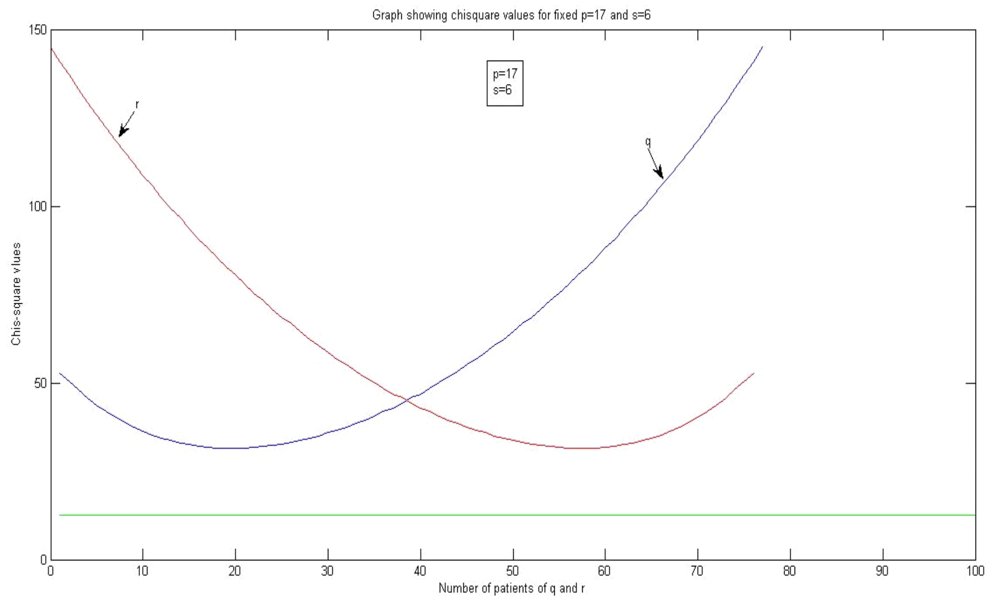

Fig.3 Graph showing chi-square values for fixed values of p=17 and q=6

Case (iv): Number of patients of type-1 and type-4 are 20 and 40

If p=20 and s=40 then the curing capacity of the drug X is not same as that of drug Y and Z for any values of q and r so that q +r =40(Fig.4). We can also observe that no values of r and q are below the line parallel to x-axis which represents tabulated Chi-square value. .

Number of patients		Chi square value	Number of patients		Chi square Value
q	r		q	r	
1	39	36.301647	21	19	37.015229
2	38	34.877734	22	18	38.344289
3	37	33.704545	23	17	39.815274
4	36	31.845144	24	16	41.938756
5	35	30.959674	25	15	43.530861
6	34	30.343706	26	14	45.317703
7	33	29.364935	27	13	47.880221
8	32	28.959091	28	12	49.706926
9	31	28.852552	29	11	51.799590

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10	30	28.552995	30	10	54.814069
11	29	28.580902	31	9	56.855556
12	28	28.949784	32	8	59.246970
13	27	29.186093	33	7	62.732468
14	26	29.611688	34	6	64.975663
15	25	30.432899	35	5	67.661378
16	24	31.101748	36	4	71.643292
17	23	31.896583	37	3	74.080526
18	22	33.156016	38	2	77.058467
19	21	34.182323	39	1	81.568939
20	20	35.323990	40	0	84.196970

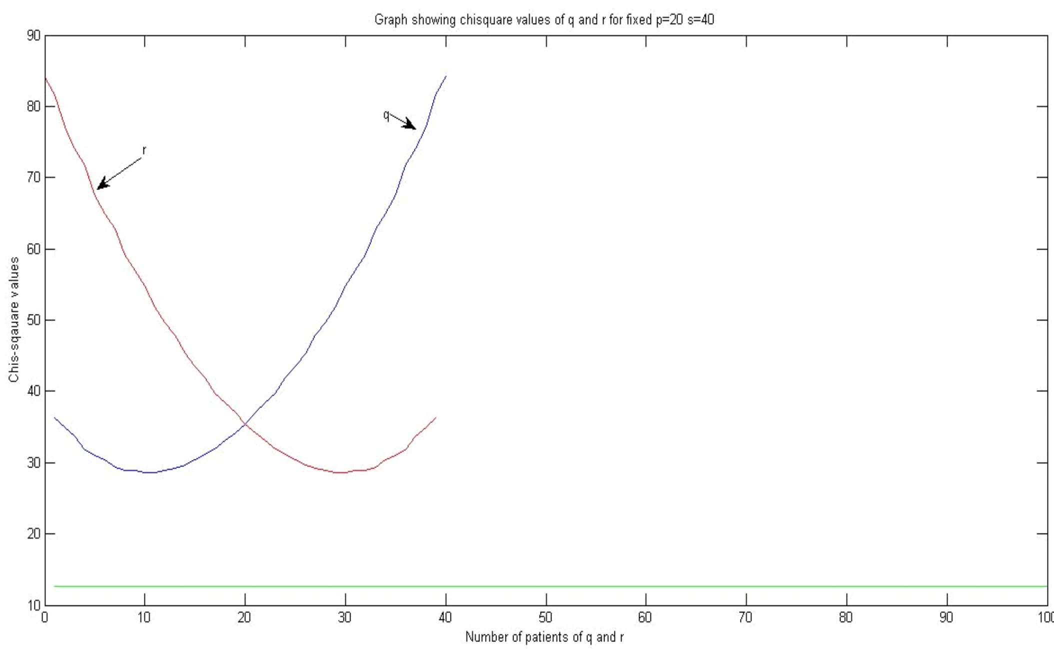

Fig.4 Graph showing chi-square values for fixed values of p=20 and q=40

The following is a Matlab program which accept the input values p,q,r,s and gives the output whether the drug is one par with other two medicines/drugs

```
function result= ksmvalue(x)
po =x(1,1);qo= x(1,2);ro=x(1,3);so=x(1,4);
yo=[2 16 53 29];zo=[7 18 46 29];xo=[po qo ro so];
totxo=sum(xo);totyo=sum(yo);totzo=sum(zo);
for i=1:4
type1sum(i)=xo(i)+yo(i)+zo(i);
end
```

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```
gt=totxo+totyo+totzo;xe=round(type1sum*totxo/gt);
ye=round(type1sum*totyo/gt);ze=round(type1sum*totzo/gt);
rowchix2=(xo-xe).^2./xe;rowchiy2=(yo-ye).^2./ye;
rowchiz2=(zo-ze).^2./ze;
chi2xyz=rowchix2+rowchiy2+rowchiz2;
chi2=sum(chi2xyz);
fprintf('chisquare value is %10.4f\n',chi2);
if (chi2<12.59)
   result=1;
  fprintf('x drug is on par with y and z\n');
 else
    result=0;
     fprintf('x drug is not  on par with y and z\n');
 end
```

Method of execution:

Step1:wite the following at matlab prompt
ksmvalue([2 13 35 50])
Step2: press enter key
OUTPUT OF THE PROGRAM WILL BE SHOWN AT MATLAB PROMPT.

References:

[1]: Spina, D.,"Statistics in Pharmacology",British Journal of Pharmacology,2007,152(3),pp 291-293.
[2]:Winder, C.V.,"Some examples of the use of Statistics in Pharmacology,1950,Annals of the New York Academy of Sciences.
[3]: Sambaiah,K. et.al. Mathematical modeling for estimation of probability of there being n bacteria at time t in two parameter ,Int. Journal of Innovation in science and mathematics, vol. 3 issue 2, ISSN(on line) 2347-9051(2014).
[4]: James M. Ritter,Lionel D.Lewis, Timothy G.K. Mant, Albert Ferro ,"A text book of clinical Pharmacologym 5th edition 2008, Hoarder Amold, London
[5]: Gupta S.C. and Kapoor V.K. "Fundamentals of Mathematical Statistics",10th edition, Sultan Chand & sons, New Delhi India.