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The Insulin Bio Intervals

Antifertility Activity

Highlights

Hepatoprotective Activities

Indian Medicinal Plants

Discovering Thoughts, Inventing Future

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The Insulin Bio Intervals

By Lutvo Kurić
Centro Universitário Feevale

Abstract - The modern science mainly treats the biochemical basis of sequencing in bio-macromolecules and processes in medicine and biochemistry. One can ask weather the language of biochemistry is the adequate scientific language to explain the phenomenon in that science. Is there maybe some other language, out of biochemistry, that determines how the biochemical processes will function and what the structure and organization of life systems will be? The research results provide some answers to these questions. They reveal to us that the process of sequencing in bio-macromolecules is conditioned and determined not only through biochemical, but also through cybernetic and information principles. Many studies have indicated that analysis of protein sequence codes and various sequence-based prediction approaches, such as predicting drug-target interaction networks (He et al., 2010), predicting functions of proteins (Hu et al., 2011; Kannan et al., 2008), analysis and prediction of the metabolic stability of proteins (Huang et al., 2010), predicting the network of substrate-enzyme-product triads (Chen et al., 2010), membrane protein type prediction (Cai and Chou, 2006; Cai et al., 2003; Cai et al., 2004), protein structural class prediction (Cai et al., 2006; Ding et al., 2007), protein secondary structure prediction (Chen et al., 2009; Ding et al., 2009b), enzyme family class prediction (Cai et al., 2005; Ding et al., 2009a; Wang et al., 2010), identifying cyclin proteins (Mohabatkar, 2010), protein subcellular location prediction (Chou and Shen, 2010a; Chou and Shen, 2010b; Kandaswamy et al., 2010; Liu et al., 2010), among many others as summarized in a recent review (Chou, 2011), can timely provide very useful information and insights for both basic research and drug design and hence are widely welcome by science community. The present study is attempted to develop a novel sequence-based method for studying insulin in hopes that it may become a useful tool in the relevant areas.

Keywords : *human insulin, algorithm, insulin model, insulin code, bio interval.*

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The Insulin Bio Intervals

Lutvo Kurić

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Keywords : human insulin, algorithm, insulin model, insulin code, bio interval.

I. Introduction

The biologic role of any given protein in essential life processes, eg, insulin, depends on the positioning of its component amino acids, and is understood by the „positioning of letters forming words“. Each of these words has its biochemical base. If this base is expressed by corresponding discrete numbers, it can be seen that any given base has its own program, along with its own unique cybernetics and information characteristics.

Indeed, the sequencing of the molecule is determined not only by distin biochemical features, but also by cybernetic and information principles. For this reason, research in this field deals more with the quantitative rather than qualitative characteristcs of genetic information and its biochemical basis. For the purposes of this paper, specific physical and chemical factors have been selected in order to express the genetic information for insulin.Numerical values are them assigned to these factors, enabling them to be measured. In this way it is possible to determine oif a connection really exists between the quantitative ratios in the process of transfer of genetic information and the qualitative appearance of the insulin molecule. To select these factors, preference is given to classical physical and chemical parameters, including the number of atoms in the relevant amino acids, their analog values, the position in these amino acids in the peptide chain, and their frenquencies.There is a arge numbers of these parameters, and each of their gives important genetic information. Going through this process, it becomes clear that there is a mathematical relationship between quantitative ratios and the qualitative appearance of the biochemical „genetic processes“ and that there is a measurement method that can be used to describe the biochemistry of insulin.

II. Methods

The biologic role of any given protein in essential life processes, eg, insulin, depends on the positioning of its component amino acids, and is understood by the „positioning of letters forming words“. Each of these words has its biochemical base. If this base is expressed by corresponding discrete numbers, it can be seen that any given base has its own program, along with its own unique cybernetics and information characteristics. Indeed, the sequencing of the molecule is determined not only by distin biochemical features, but also by cybernetic and information principles. For this reason, research in this field deals more with the quantitative rather than qualitative characteristcs of genetic information and its biochemical basis. For the purposes of this paper, specific physical and chemical factors have been selected in order to express the genetic information for insulin. Numerical values are them assigned to these factors, enabling them to be measured. In this way it is possible to determine oif a connection really exists between the quantitative ratios in the process of transfer of genetic information and the qualitative appearance of the insulin molecule. To select these factors, preference is given to classical physical and chemical parameters, including the number of atoms in the relevant amino acids, their analog values, the position in these amino acids in the peptide chain, and their frenquencies. There is a arge numbers of these parameters, and each of their gives important genetic information. Going through this

process, it becomes clear that there is a mathematical relationship between quantitative ratios and the qualitative appearance of the biochemical „genetic processes“ and that there is a measurement method that can be used to describe the biochemistry of insulin.

Insulin can be represented by two different forms, ie, a discrete form and a sequential form. In the discrete form, a molecule of insulin is represented by a set of discrete codes or a multiple dimension vector. In the sequential form, an insulin molecule is represent by a series of amino acids according to the order of their position in the chains 1AI0.

Therefore, the sequential form can naturally reflect all the information about the sequence order and lenght of an insulin molecule. The key issue is whether we can develop a different discrete method of representing an insulin molecule that will allow accomodation of partial, if not all sequence order information? Because a protein sequence is usually represented by a series of amino acids should be assigned to these codes in order to optimally convert the sequence order information into a series of numbers for the discrete form representation?

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Therefore, the sequential form can naturally reflect all the information about the sequence order and lenght of an insulin molecule. The key issue is whether we can develop a different discrete method of representing an insulin molecule that will allow accomodation of partial, if not all sequence order information? Because a protein sequence is usually represented by a series of amino acids should be assigned to these codes in order to optimally convert the sequence order information into a series of numbers for the discrete form representation?

III. Expression of Insulin Code Matrix- 1ai0

The matrix mechanism of Insulin, the evolution of biomacromolecules and, especially, the biochemical evolution of Insulin language, have been analyzed by the application of cybernetic methods, information theory and system theory, respectively. The primary structure of a molecule of Insulin is the exact specification of its atomic composition and the chemical bonds connecting those atoms.

R6 INSULIN HEXAMER (d1ai02)

The structure 1AI0 has in total 12 chains. Out of these 2 are sequence-unique

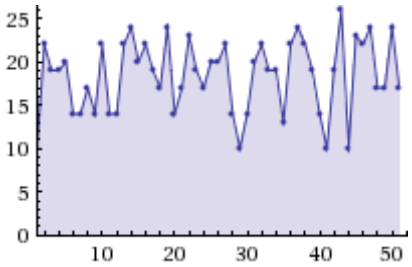
>1AI0:A		GIVEQCCTSICSLYQLENYCN
>1AI0:B		FVNQHLCGSHLVEALYLVCGERGFFYTPKT
>1AI0:C		GIVEQCCTSICSLYQLENYCN
>1AI0:D		FVNQHLCGSHLVEALYLVCGERGFFYTPKT
>1AI0:E		GIVEQCCTSICSLYQLENYCN
>1AI0:F		FVNQHLCGSHLVEALYLVCGERGFFYTPKT
>1AI0:G		GIVEQCCTSICSLYQLENYCN
>1AI0:H		FVNQHLCGSHLVEALYLVCGERGFFYTPKT
>1AI0:I		GIVEQCCTSICSLYQLENYCN
>1AI0:J		FVNQHLCGSHLVEALYLVCGERGFFYTPKT
>1AI0:K		GIVEQCCTSICSLYQLENYCN
>1AI0:L		FVNQHLCGSHLVEALYLVCGERGFFYTPKT

G	I	V	E	Q	C	C	T	S	I	C	S	L	Y	Q	L	E
10	22	19	19	20	14	14	17	14	22	14	14	22	24	20	22	19
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
N	Y	C	N	F	V	N	Q	H	I	C	G	S	H	L	V	E
17	24	14	17	23	19	17	20	20	22	14	10	14	20	22	19	19
18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
A	L	Y	L	V	C	G	E	R	G	F	I	Y	T	P	K	T
13	22	24	22	19	14	10	19	26	10	23	22	24	17	17	24	17
35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51

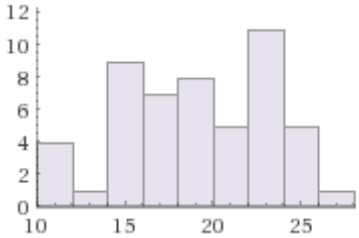
Input:

{10, 22, 19, 19, 20, 14, 14, 17, 14, 22, 14, 14, 22, 24, 20, 22, 19,
17, 24, 14, 17, 23, 19, 17, 20, 20, 22, 14, 10, 14, 20, 22, 19, 19,
13, 22, 24, 22, 19, 14, 10, 19, 26, 10, 23, 22, 24, 17, 17, 24, 17}

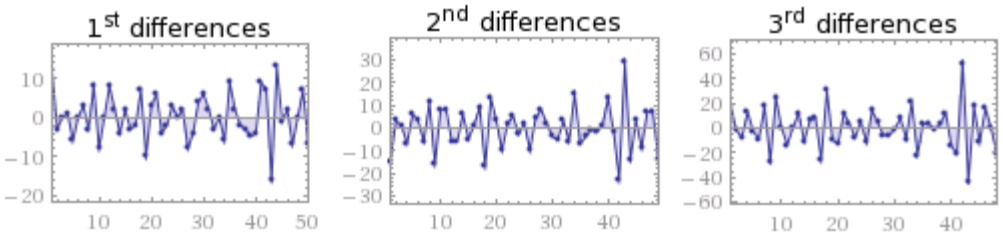
Plot:



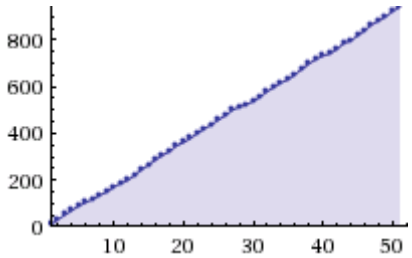
Histogram:



Differences:



Cumulative sums:



As wesee, the genetic information characterized only by biochemical, or also by cyberinformation principles

Fragment 1

From 1 to 102

G	I	V	E	Q	C	C		T
10	22	19	19	20	14	14	...	17
1	2	3	4	5	6	7		102

Fragment 2

From 103 to 204

G	I	V	E	Q	C	C		T
10	22	19	19	20	14	14	…	17
103	104	105	106	107	108	109		204

Fragment 3

From 205 to 306

G	I	V	E	Q	C	C		T
10	22	19	19	20	14	14	…	17
205	206	207	208	209	210	211		306

Aforementioned aminoacids are positioned from number 1 to 306. Numbers 1, 2, 3, n... present the position of a certain aminoacid. This positioning is of the key importance for understanding of programmatic, cybernetic and information principles in this protein. The scientific key for interpretation of bio chemical processes is the same for insulin and as well as for the other proteins and other sequences in biochemistry. The first aminoacid in this example has 10 atoms, the second one 22, the third one 19, etc... Why do they have exactly this many atoms? It is because there are many codes in the molecule of insulin, analogue codes and other coded features. In fact, there is a program-cybernetic algorithm in which it is „recorded" that the firs amino acid has to have 10 atoms, the second one 22, the third one 19, etc... The first amino acid has its own biochemistry, the second and the third one also. The conclusion here has to be that there is a concrete relationship between quantitative ratios in the process of transfer of genetic information and qualitative appearance, i.e. the characteristics of organisms.

ALGORITHM

We shall now give some mathematical evidences that will prove that in the biochemistry of insulin there really is programmatic and cybernetic algorithm in which it is „recorded", in the language of mathematics, how the molecule will be built and what will be the quantitative characteristics of the given genetic information.

Step 1 (From 1 to 306)

$$R1 = 10;\ R2 = 22;\ R3 = 19;\ldots\ R306 = 17;$$

$$[R1 + (R1+R2) + (R1+R2+R3)\ldots, + (R1+R2+R3\ldots, + R306)] = S;$$

$$R1 = 10 \text{ atoms};$$

$$(R1+R2) = (10+22) = 32;$$
$$(R1+R2+R3) = (10+22+19) = 51;$$
$$(R1+R2+R3\ldots, + R306) = 5640 \text{ atoms};$$
$$R1,2,3,n = \text{Number of atoms in amino acids } 1,2,3,n$$

$$[R1 + (R1+R2) + (R1+R2+R3)\ldots, + (R1+R2+R3\ldots, + R306)] =$$
$$= (10+32+51+70\ldots, + 5640) = S;$$
$$S = 863\ 208;$$

Step 2 (From 306 to 1)

$$R306 = 17;\ R305 = 24;\ R304 = 17;\ldots\ R1 = 10 \text{ atoms};$$

$$[R306 + (R306+R305) + (R306+R305+R304)\ldots, + (R306+R305+R304\ldots, + R1)] = S1;$$

$$R306 = 17;$$
$$(R306+R305) = (17+24) = 41;$$
$$(R306+R305+R304) = (17+24+17) = 58;$$
$$(R306+R305+R304\ldots, + R1) = (17+24+17\ldots, + 10) = 5640;$$

R1,2,3,n = Number of atoms in amino acids 1,2,3,n

[R306 + (R306+R305) + (R306+R305+R304)..., + (R306+R305+R304..., + R1)] =
= (17+41+58+75…, + 5640) = S1;
S1 = 868 272;

From 1 to 102 and from 102 to 1

	G	I	V	E	Q	C	C	.	.	T	SUM
	10	22	19	19	20	14	14	.	.	17	1880
	1	2	3	4	5	6	7	.	.	102	5253
Step 1	10	32	51	70	90	104	118	.	.	1880	95976
Step 2	5640	5630	5608	5589	5570	5550	5536	.	.	3777	481184
											577160

(0+10) = 10; (10+22)=32; (10+22+19)=51; etc.
(17+24+17..., + 10) = 5640; (17+24+17..., + 22) = 5630; etc.
(95976 + 481184) = 577160:

From 103 to 204 and from 204 to 103

	G	I	V	E	Q	C	C	.	.	T	SUM
	10	22	19	19	20	14	14	.	.	17	1880
	103	104	105	106	107	108	109	.	.	204	15657
Step 1	1890	1912	1931	1950	1970	1984	1998	.	.	3760	287736
Step 2	3760	3750	3728	3709	3690	3670	3656	.	.	1897	289424
											577160

(287736 + 289424) = 577160;

From 205 to 306 and from 306 to 205

	G	I	V	E	Q	C	C	.	.	T	SUM
	10	22	19	19	20	14	14	.	.	17	1880
	205	206	207	208	209	210	211	.	.	306	26061
Step 1	3770	3792	3811	3830	3850	3864	3878	.	.	5640	479496
Step 2	1880	1870	1848	1829	1810	1790	1776	.	.	17	97664
											577160

(479496 + 97664) = 577160;

From 1 to 102		From 103 to 204		From 205 to 306
↓		↓		↓
577160		577160		577160
↘		↓		↙
		1.731.480		

1.731.480 = (5640+5640+5640... + 5640);

Number of atoms in Insulin = 5640;

Schematic representation of the bio intervals from 1 to 306 we will show in the fig.1 and 2.

In that group of chains there are three groups with 102 amino acids. Each of these three groups of amino acids has an identical number of atoms.

It can be concluded that there is a connection between quantitative characteristics in the process of transfer of genetic information and the qualitative appearance of given genetic processes.

BIO INTERVALS – AMINO ACIDS FROM 1 TO 306

Within the digital pictures in biochemistry, the physical and chemical parameters are in a strict compliance with programmatic, cybernetic and information principles. As an example, we will here give you the mathematical gravity forces. These forces determine the positioning of aminoacids in their molecules. Each bar in the protein chain attracts only the corresponding aminoacid, and only the relevant aminoacid can be positioned at certain place in the chain. Each peptide chain can have the exact number of aminoacids necessary to meet the strictly determined mathematical conditioning. It can have as many atoms as necessary to meet the mathematical balance of the biochemical phenomenon at certain mathematical level, etc... the digital language of biochemistry has a countless number of codes and analogue codes, as well as other information content. These pictures enable us to realize the very essence of functioning of biochemical processes.

Insulin Bio Intervals(1)

Step 1

Number of atoms	Bio intervals	Rank	Number of atoms	Bio intervals	Rank	Number of atoms	Bio intervals	Rank
199 From 1 to 12	199	78	1139 From 1 to 63	199	2016	2079 From 1 to 114	199	6555
323 From 1 to 18	124	171	1263 From 1 to 69	124	2415	2203 From 1 to 120	124	7260
361 From 1 to 20	38	210	1301 From 1 to 71	38	2556	2241 From 1 to 122	38	7503
579 From 1 to 32	218	528	1519 From 1 to 83	218	3486	2459 From 1 to 134	218	9045
617 From 1 to 34	38	595	1557 From 1 to 85	38	3655	2497 From 1 to 136	38	9316
741 From 1 to 41	124	861	1681 From 1 to 92	124	4278	2621 From 1 to 143	124	10296
940 From 1 to 51	199	1326	1880 From 1 to 102	199	5253	2820 From 1 to 153	199	11781
3760	940		10340	940		16920	940	

(199-0) = 199; (323-199) = 124; (361-323) = 38; (741-617) = 124;
(940-741) = 199; (1139-940) = 199; (1263-1139) = 124;
etc.

(Chain A + Chain B) = 940 atoms,
(Chain C + Chain D) = 940 atoms,
etc.

(3760 + 16920) = (10340 + 10340);
10340 = (940+940+940.., + 940);

3760 = (940+940+940+940)
10340 = (940+940+940..., + 940)
16920 = (940+940+940..., + 940)

(2079-1139) = (1139-199);
(2203-1263) = (1263-323);
(2241-1301) = (1031-361);
etc.

Correlation of bio intervals

Number of atoms	Bio intervals	Number of atoms	Bio Intervals	Number of atoms	Bio Intervals
199	199	1139	199	2079	199

[(199 + 2079) : 2] = 1139;

Number of atoms	Bio intervals	Number of atoms	Bio Intervals	Number of atoms	Bio Intervals
323	124	1263	124	2203	124

[(323 + 2203) : 2] = 1263;

Number of atoms	Bio intervals	Number of atoms	Bio Intervals	Number of atoms	Bio Intervals
361	38	1301	38	2241	38

[(361 + 2241): 2] = 1301;

Number of atoms	Bio intervals	Number of atoms	Bio Intervals	Number of atoms	Bio Intervals
579	218	1519	218	2459	218

[(579 + 2459) : 2] = 1519;

Number of atoms	Bio intervals	Number of atoms	Bio Intervals	Number of atoms	Bio Intervals
617	38	1557	38	2497	38

[(617 + 2497) : 2] = 1557;

Number of atoms	Bio intervals	Number of atoms	Bio Intervals	Number of atoms	Bio Intervals
741	124	1681	124	2621	124

[(741 + 2621) : 2] = 1681;

Number of atoms	Bio intervals	Number of atoms	Bio Intervals	Number of atoms	Bio Intervals
940	199	1880	199	2820	199

[(940 + 2820) : 2] = 1880;

Insulin Bio Intervals(2)

Number of atoms	Bio intervals	Rank	Number of atoms	Bio intervals	Rank	Number of atoms	Bio intervals	Rank
3019 From 1 to 165	199	13695	3959 From 1 to 216	199	23436	4899 From 1 to 267	199	35778
3143 From 1 to 171	124	14706	4083 From 1 to 222	124	24753	5023 From 1 to 273	124	37401
3181 From 1 to 173	38	15051	4121 From 1 to 224	38	25200	5061 From 1 to 275	38	37950
3399 From 1 to 185	218	17205	4339 From 1 to 236	218	27966	5279 From 1 to 287	218	41328
3437 From 1 to 187	38	17578	4377 From 1 to 238	38	28441	5317 From 1 to 289	38	41905
3561 From 1 to 194	124	18915	4501 From 1 to 245	124	30135	5441 From 1 to 296	124	43956
3760 From 1 to 204	199	20910	4700 From 1 to 255	199	32640	5640 From 1 to 306	199	46971
23500	940		30080	940		36660	940	

(3019-2820) = 199; (3143-3019) = 124; (3181-3143) = 38; etc.

Schematic representation of the bio intervals from 199 to 5640 we will show in the fig.3.

Correlation of bio intervals

Number of atoms	Number of atoms	Number of atoms
3019	3959	4899

(3019 + 4899) = (3959 x 2);

Number of atoms	Number of atoms	Number of atoms
3143	4083	5023

(3143 + 5023) = (4083 x 2);

Number of atoms	Number of atoms	Number of atoms
3181	4121	5061

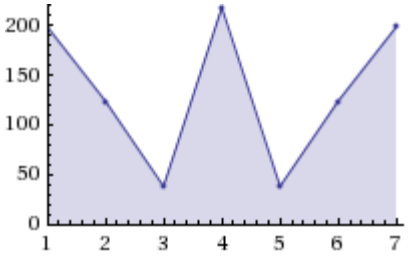
(3181 + 5061) = (4121 x 2); etc.

The molecule of insulin we can understand as words built from letters, i.e. aminoacids. The meaning of words is determined by positioning of letters. Each of these words has its biochemical base. If this base is expressed by corresponding discrete numbers, we find out that the base has its own program, cybernetic and information characteristics. In fact, we will find out that the sequencing of the molecule is conditioned and determined not only by biochemical, but also by cybernetic and information principles.

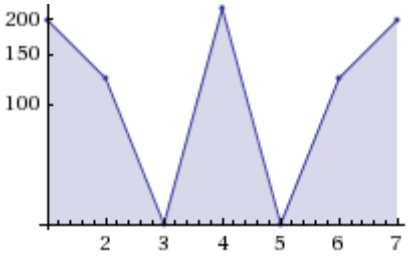
BIO INTERVALS(3)

Mathematica plaintext input:

Plot:



Long-linear plot:



ListLogPlot[{199, 124, 38, 218, 38, 124, 199}, Joined -> True, Mesh -> All, Filling -> Axis]

BIO INTERVAL – AMINO ACIDS-FROM 306 TO 1.

Step 2

Number of atoms	Bio intervals	Rank	Number of atoms	Bio intervals	Rank	Number of atoms	Bio Intervals	Rank
199 From 306 to 297	199	3015	1139 From 306 to 246	199	16836	2079 From 306 to 195	199	28056
323 From 306 to 290	124	5066	1263 From 306 to 239	124	18530	2203 From 306 to 188	124	29393
361 From 306 to 288	38	5643	1301 From 306 to 237	38	19005	2241 From 306 to 186	38	29766
579 From 306 to 276	218	9021	1519 From 306 to 225	218	21771	2459 From 306 to 174	218	31920
617 From 306 to 274	38	9570	1557 From 306 to 223	38	22218	2497 From 306 to 172	38	32265
741 From 306 to 268	124	11193	1681 From 306 to 217	124	23535	2621 From 306 to 166	124	33276
940 From 306 to 256	199	14331	1880 From 306 to 205	199	26061	2820 From 306 to 154	199	35190
3760	940		10340	940		16920	940	

[(199 + 2079) : 2] = 1139; [(323 + 2203) : 2] = 1263; etc.

Schematic representation of the bio intervals from 306 to 1 we will show in the fig.4.

Step 2

199	199
323	124
361	38
579	218
617	38
741	124
940	199
3760	940

1139	199
1263	124
1301	38
1519	218
1557	38
1681	124
1880	199
10340	940

2079	199
2203	124
2241	38
2459	218
2497	38
2621	124
2820	199
16920	940

3019	199
3143	124
3181	38
3399	218
3437	38
3561	124
3760	199
23500	940

3959	199
4083	124
4121	38
4339	218
4377	38
4501	124
4700	199
30080	940

4899	199
5023	124
5061	38
5279	218
5317	38
5441	124
5640	199
36660	940

(323-199) = 124; (361-323) = 38; (579-361) = 218; etc.

(36660 + 3760) + (30080 + 10340) + (23500 + 16920) = (940 x Y);

Y = 43;

Connection:

(36660 and 3760) > 36660 3760 = (940 x Y1);
(3760 and 36660) > 3760 36660 = (940 x Y2);
(30080 and 10340) > 30080 10340 = (940 x Y3);
(10340 30080) >10340 30080 = (940 x Y4);
(23500 and 16920) > 23500 16920 = (940 x Y5);
(16920 and 23500) > 16920 23500 = (940 x Y5);

In those examples there is an exact mathematical balance of groups of aminoacids from 1 to 102, 103 to 204, 205 to 306 and 199 to 5640.. This balance is one of important quantitative characteristics of all processes in biochemistry. How functioning of biochemistry is determined through cybernetic information principles, will be discussed further in Table 1.

BIO INTERVALS(4)

The result of the research that we have carried out clearly shows that there is a matrix code in insulin. It also shows that the coding system within the amino acidic language gives a full information, not only for the amino acid „record“, but also for its structure, configuration and its various shapes. In the following text we shall discuss the issue of the existence of the insulin code, and also the issue of coding of individual structural levels in this protein.

BIO INTERVAL (+)199

Impulse 1				Impulse 2
G	I	V		S
10	22	19	…	14
1	2	3	…	12
10	32	51	…	199
5640	5630	5608	…	5455

(10+22+19…, + 14) = 199;

BIO INTERVAL (-)199

Impulse -2				Impulse -1
E		T	P	K	T
19	…	17	17	24	17
297	…	303	304	305	306
5460	…	5582	5599	5623	5640
199	…	75	58	41	17

BIO INTERVAL (+)323

Impulse 1				Impulse 3
G	I	V		N
10	22	19	…	17
1	2	3		18
10	32	51		323
5640	5630	5608		5334

BIO INTERVAL (-)323

Impulse -3				Impulse -1
A		T	P	K	T
13	…	17	17	24	17
290		303	304	305	306
5330		5582	5599	5623	5640
323		75	58	41	17

BIO INTERVAL (+)361

Impulse 1				Impulse 4
G	I	V		C
10	22	19	…	14
1	2	3		20
10	32	51		361
5640	5630	5608		5293

BIO INTERVAL (-)361

Impulse-4				Impulse –1
V		T	P	K	T
19	…	17	17	24	17
288		303	304	305	306
5298		5582	5599	5623	5640
361		75	58	41	17

etc.

The molecule of insulin we can understand as words built from letters, i.e. aminoacids. The meaning of words is determined by positioning of letters. Each of these words has its biochemical base. If this base is expressed by corresponding discrete numbers, we find out that the base has its own program, cybernetic and information characteristics. In fact, we will find out that the sequencing of the molecule is conditioned and determined not only by biochemical, but also by cybernetic and information principles.

BIO INTERVAL – AMINO ACIDS-FROM 1 to 306 and 306 TO 1.

Bio intervals of insulin we will show in the table 1 and table 2.

Step 1

Table 1 : Bio intervals (from 1 to 306)

199	323	361	579	617	741	940
1139	1263	1301	1519	1557	1681	1880
2079	2203	2241	2459	2497	2621	2820
3019	3143	3181	3399	3437	3561	3760
3959	4083	4121	4339	4377	4501	4700
4899	5023	5061	5279	5317	5441	5640

(1139 -199) = (2079-1139) = (3019-2079); etc.

Step 2

Table 2 : Bio intervals (from 306 to 1)

940	741	617	579	361	323	199
1880	1681	1557	1519	1301	1263	1139
2820	2621	2497	2459	2241	2203	2079
3760	3561	3437	3399	3181	3143	3019
4700	4501	4377	4339	4121	4083	3959
5640	5441	5317	5279	5061	5023	4899

(1880-940) = 2820-1880); etc.

These tables contains an overview of all bio intervals. The bio intervals show some of the quantitative characteristics of the molecule of insulin.

Schematic representation of the bio intervals we will show in the fig.5, 6 and 7.

The Insulin Bio Signal Code

We shall now give some mathematical evidences that will prove that in the biochemistry of insulin there really is programmatic and cybernetic algorithm in which it is „recorded“, in the language of mathematics, how the molecule will be built and what will be the quantitative characteristics of the given genetic information.

	Signal +199	Signal -5441	
	S	L	Y
14	14	22	24
11	12	13	14
185	199	221	245
5469	5455	5441	5419

(199 + 5441) = 5640;

Signal +323	Signal -5317	Signal +361	Signal -5279		
E	N	Y	C	N	F
19	17	24	14	17	23
17	18	19	20	21	22
306	323	347	361	378	401
5353	5334	5317	5293	5279	5262

(323+5317) = 5640; (361+5279) = 5640; (361-323) = (5317 – 5279)

	Signal +579	Signal -5061	Signal +617	Signal -5023	
H	L	V	E	A	L
20	22	19	19	13	22
31	32	33	34	35	36
557	579	598	617	630	652
5103	5083	5061	5042	5023	5010

(579+5061) = (617+5023) (617-579) = (5061 – 5023)

	Signal +741	Signal -4899	
C	G	E	R
14	10	19	26
40	41	42	43
731	741	760	786
4923	4909	4899	4880

(741 + 4899) = 5640;

	Signal +940	Signal -4700	
K	T	G	I
24	17	10	22
50	51	52	53
923	940	950	972
4741	4717	4700	4690

(4700 + 940) = 5640; etc.

Aforementioned bio-codes were calculated using of corresponding groups of aminoacids. These are unions with different number of aminoacids. There are different ways and methods of selecting these unions of amino acids. We hope that science will determine which method is most efficient for this selection. Some signals have a positive, and some have negative numeric value.

IV. Discussion

The results of our research show that the processes of sequencing the molecules are conditioned and arranged not only with chemical and biochemical lawfulness, but also with program, cybernetic and informational lawfulness too. At the first stage of our research we replaced nucleotides from the Amino Acid Code Matrix with numbers of the atoms in those nucleotides. Translation of the biochemical language of these amino acids into a digital language may be very useful for developing new methods of predicting protein sub-cellular localization, membrane protein type, protein structure secondary prediction or any other protein attributes. Since the concept of Chou's pseudo amino acid composition was proposed [1,2], there have been many efforts to try to use various digital numbers to represent the 20 native amino acids in order to better reflect the sequence-order effects through the vehicle of pseudo amino acid composition. Some investigators used complexity measure factor [3], some used the values derived from the cellular automata [4-7], some used hydrophobic and/or hydrophilic values [8-16], some were through Fourier transform [17,18], and some used the physicochemical distance [19]. The author [34-40] is devoted to provide a digital code for each of 20 native amino acids. These digital codes should more complete and better reflect the essence of each of the 20 amino acids. Therefore, it might stimulate a series of future work by using the author's digital codes to formulate the pseudo amino acid composition for predicting protein structure class [20-22], subcellular location [23, 24], membrane protein type [9, 25], enzyme family class [26, 27], GPCR type [28, 29], protease type [30], protein-protein interaction [31], metabolic pathways [32], protein quaternary structure [33], and other protein attributes. It is going to be possible to use a completely new strategy of research in genetics in the future. However, close observation of all these relationships, which are the outcomes of periodic laws (more specifically the law of binary coding), stereo-chemical and digital structure of proteins.

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Awards

Gold medal for Bosnia and Herzegovina, in the name of your people and Bosnia and Herzegovina. Such individuals deserve recognition not only within their country of origin, but also worldwide. As such, the American Biographical Institute – a highly esteemed leader in the research of upstanding individuals around the globe – has selected you to receive one of its most internationally prominent honors, the GOLD MEDAL FOR BOSNIA AND HERZEGOVINA. –International health professional of the year 2010., -Man of the year in medicine and healthare designation for 2010.,-The international Hipocrates awards for medical achievement, -Cambridge certificate for outstanding medical achievement for 2011. – International health professional of the year 2012.-Cambridge certificate for Outstanding Medical Achievement, 2012., -ABI-Man of the year 2012. - Nomination for Great Minds of the 21st Century, a major reference directory including just 1.000 of the world's top thinkers and intellectuals. My contributions to the field of medicine and healthcare have waranted the high regard of nomination for Great Minds of the 21st Century.

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Comparative Hepatoprotective Activities of Selected Indian Medicinal Plants

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Abstract - The present study deals with comparative evaluation of hepatoprotective activities of Melia azedarach Linn, Catharanthus Rosea and Brassica oleracea L.var.capitata ethanolic leaves extracts against simvastatin induced hepatotoxicity in rats. Hepatotoxicity in rats was induced by simvastatin (20 mg/kg p.o. for 30 days) and the protective effect of Melia azedarach Linn, Catharanthus Rosea and Brassica oleracea L.var.capitata (300 mg/kg/p.o. and 500 mg/kg/p.o.) was identified by estimating marker enzymes. Simvastatin treated rats shows significant changes in biochemical parameters i.e. increases in Serum Glutamate Pyruvate Transaminase (SGPT), Serum Glutamate Oxaloacetate Transaminase (SGOT), Alanine Phosphatase (ALP), Serum bilirubin and decrease in Total proteins content, which were restored towards normalization in extracts treated rats. The results revealed that the ethanolic extracts of Melia azedarach Linn, and Brassica oleracea L.var.capitata (300 mg/kg/p.o. and 500 mg/kg/p.o.) exhibited potent hepatoprotective activity than Catharanthus Rosea. The hepatoprotective effect of extracts was further confirmed by histopathological studies of liver, which shows normal architecture of liver cell than compared with hepatotoxicant group. Possible mechanism for hepatoprotective activity may be due to free radical scavenging potential in extracts.

Keywords : *melia azedarach linn, catharanthus rosea and brassica oleracea L.var.capitata, hepatoprotective activity and simvastatin.*

GJMR-B Classification : *NLMC Code: WB 55.A9*

Strictly as per the compliance and regulations of:

Comparative Hepatoprotective Activities of Selected Indian Medicinal Plants

Mohammed Fazil Ahmed [α] & A. Srinivasa Rao [σ]

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Keywords : melia azedarach linn, catharanthus rosea and brassica oleracea L.var.capitata, hepatoprotective activity and simvastatin.

I. Introduction

Liver diseases remain as one of the serious health problems. It is the key organ of metabolism and excretion. It is often exposed to variety xenobiotics and therapeutic agents.[1] Conventional drugs used in the treatment of liver diseases are often inadequate. It is therefore necessary to search for alternative drugs for the treatment of liver diseases to replace the currently used drugs of doubtful efficacy and safety. More than 900 drugs have been implicated in causing liver injury[2] and it is the most common reason for a drug to be withdrawn from the market. Drug induced liver injury is responsible for 5% of all hospital admissions and 50% of all acute liver failures.[3, 4]

Simvastatin hepatotoxicity is hypothesized to occur due to drug-drug interactions.[5, 6] Simvastatin (Lipid Lowering Agent) competitively inhibits HMG-Co A (3-hydroxy-3 methylglutaryl coenzyme A) to mevalonate. Mevalonate is also a precursor of Coenzyme Q10 (CoQ10). Thus, treatment with statins could also lower its levels. CoQ10 acts as an antioxidant, has membrane stabilising effects, and is important for cellular mitochondrial respiration, which is essential for energy production in organs.[7, 8]. Thus, simvastatin causes oxidative stress mediated hepatotoxicity by depleting antioxidant enzymes.[9] The enzymes L- alanine aminotransferase (L-ALT), L-aspartate amino transferase (L-AST), alkaline phosphatase (ALP) and lactate dehydrogenase (LDH), are often used in assessing the integrity of the liver.[10]Liver fibrosis occurs as a result of a variety of pathological factors, including viral hepatitis (especially hepatitis B and C), alcohol and drug abuse, metabolic diseases due to overload of iron or copper, autoimmunity against hepatocytes or bile duct epithelium and congenital abnormalities.[11]

Herbal drugs play a role in the management of various liver disorders most of which speed up the natural healing processes of the liver. Numerous medicinal plants and their formulations are used for liver disorders in ethnomedical practice as well as traditional system of medicine in India. Silymarin is a flavonolignan that has been introduced fairly recently as a hepatoprotective agent. Silymarin is extracted from the seeds and fruits of *Silybum marianum* and in reality is a mixture of three structural components: Silibinin, Silydianine and Silychristine. Clinical trials have shown that Silymarin exerts hepatoprotective effects in acute viral hepatitis, poisoning by Amanita *phalloides,* ethanol, paracetamol, and carbon tetrachloride. Many studies have demonstrated the beneficial hepatoprotective effects when treatment with Silymarin.[12]

Catharanthus Rosea, which is commonly known as '*Vinca rosea*' belongs to family Apocynaceae and is an important source of indole alkaloids, which are present in all plant parts. The important antineoplastic alkaloids namely Vincristine and Vinblastine are mainly present in the leaves whereas antihypertensive alkaloids such as ajmalicine, serpentine, and reserpine are reported to be present in the roots.[13] Vincristine and Vinblastine alkaloids are used in the treatment of various types of lymphoma and leukemia.[14, 15]

Melia azedarach, the Persian Lilac is popularly known as Maha neem tree and cultivated in all stations. It is a large evergreen tree found throughout India and very similar to Neem. Leaves have been shown to

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contain nimbinene, meliacin, quercetrin, quercetin-3-0-b-rutinoside, kaempferol- 3-0-b rutinoside, rutin and kaempferol-3-L-rhamno-Dglucoside.[16,17] Hot methanolic etract of *Melia azedarach* leaves contain dipentadecyl ketone, glycerol 1,3-bis-undec-9- enoate 2-dodec-9-enoate and glycerol tris-tridec-9-enoate.[18] The plant is traditionally used for the treatment of leprosy, inflammations, and cardiac disorders. Its fruits extracts possess ovicidal[19] and larvicidal activity. [20] The leaf extracts also possess antiviral [21] and antifertility activity.[22]

Brassica oleracea var. capitata (Cabbage) (Family Brassicaceae) is an excellent source of vitamin C. It also contains significant amounts of glutamine, an amino acid that has anti-inflammatory properties. Cabbage can also be included in dieting programs, as it is a low calorie food.The present study was directed to investigate the hepatoprotective activities of *Brassica oleracea L. var. capitata* against simvastatin induced hepatotoxicity**.** There are increasing evidences that increased consumption of fruits and vegetables and intake of certain non-nutrients that are present in foods reduce the risk of various pathological events such as cancer[23,24] and cardio- and cerebro-vascular diseases.[25] The vegetables are rich sources of many nutrients and antioxidant vitamins. Therefore, the objectives of present study deals with comparative evaluation of hepatoprotective activities of *Melia azedarach* Linn, *Catharanthus Rosea* and *Brassica oleracea L.var.capitata* ethanolic leaves extracts against simvastatin induced hepatotoxicity in rats.

II. Materials and Method

a) Plant collection and identification

The plant material of *Brassica oleracea var. capitata (Cabbage)* ware obtained from local market, while *Melia azedarach Linn* and *Catharanthus Rosea* were obtained from Mount Opera Garden, Near Ramoji Film City, Nalgonda Dist. The plant can be identified authenticated by Department of Botany, research office (Botanist), Anwar-ul- loom College of Pharmacy, Hyderabad.

b) Extraction

The leaves of *Melia azedarach* Linn, *Catharanthus Rosea* and *Brassica oleracea L.var.capitata* were dried under shade and powdered in a mechanical grinder. The powdered material (250gms) was extracted successively in Ethanol using Soxhlet apparatus at 55°C for 18 h. The extracts was concentrated in vacuo and kept in a vacuum dessicator for complete removal of solvent and weighed.

c) Experimental Animals

Wistar albino rats (150-200 g) of both sexes were obtained from the animal house of NIZAM INSTITUTE OF PHARMACY, Deshmukhi, Ramoji film city, Hyderabad. Before and during the experiment, rats were fed with standard diet (Gold Moher, Lipton India Ltd). After randomization into various groups and before initiation of experiment, the rats were acclimatized for a period of 7 days under standard environmental conditions of temperature, relative humidity, and dark/light cycle. Animals described as fasting were deprived of food and water for 16 h ad libitum. All animal experiment were carried out in accordance with the guidelines of CPCSEA and study was approved by the IAEC (Institutional animal ethical committee).

d) Acute toxicity studies of extracts

Acute oral toxicity was performed as per Organiza-tion for Economic Co-operation and Development (OECD)-423 guidelines.[26] Three male Wistar rats weighing between 150–200 g were used for each dose. The dose levels of 5 mg, 50 mg, 500 mg, 1000 mg, 2000 mg, and 5000 mg/kg/body weight, per os were selected. The lethal dose (LD)-50 value of the extract was determined. The drug was administered orally to rats, which were fasted overnight with water ad libitum before the administration of the drug. The body weight of the rat was noted before and after treatment. The animals were observed for toxic symptoms, such behavioral changes, loco-motion, convulsions, and mortality for 72 hours.

e) Experimental design for hepatoprotective activity[27]

Nine groups of rats, six in each received the following treatment schedule.

Group I : Normal control (saline)
Group II : Simvastatin (SMT) (20mg/kg.p.o)
Group III : Simvastatin (20mg/kg.p.o) + *Melia azedarach* leaf extract (300mg/kg, p.o)
Group IV : Simvastatin (20mg/kg.p.o)+*Melia azedarach* leaf extract (500mg/kg, p.o)
Group V : Simvastatin (20mg/kg.p.o) + *Catharanthus roseus* leaf extract (300mg/kg, p.o)
Group VI : Simvastatin (20mg/kg.p.o) + *Catharanthus roseus* leaf extract (500mg/kg, p.o)
Group VII: Simvastatin (20mg/kg.p.o) + *Brassica oleracea L.* var *capitata* leaf extract (300mg/kg, p.o)
Group VIII: Simvastatin (20mg/kg.p.o) + *Brassica oleracea L.* var *capitata* leaf extract (500mg/kg, p.o)
Group IX : Simvastatin (20mg/kg.p.o) +Silymarin (25mg/kg, p.o)

Animals were divided into nine different groups, each having 6 rats and treated accordingly. Group 1: rats fed with a normal standard diet for 30 days; Group II rats receives Simvastatin (SMT) (20mg/kg.p.o alone for 30 days); Group III and IV rats receive SMT along with *Melia azedarach* leaf extracts(300mg/kg and 500mg/kg.p.o respectively for 30days); Group V and VI rats receives SMT along with *Catharanthus roseus* leaf extract (300mg/kg and 500mg/kg p.o respectively for 30days); Group VII and VIII rats received SMT along with *Brassica oleracea* leaf extracts (300mg/kg and

500mg/kg p.o respectively for 30days) and Group IX rats receive SMT along with silymarin (20 mg/kg/p.o.for 30 days).

f) Blood Biochemistry

Blood samples were collected in glass tube from retro-orbital puncture to obtain haemolysis free clear serum for the analysis of SGOT and SGPT [28], ALP [29] and bilirubin [30] by standard method. Serum total protein was measured according to the method of Lowry et al, 1951. [31]

g) Histopathology

Histopathology of liver was carried out by a modified Luna (Luna LG., 1999) [32]. In brief, the autopsied livers were washed in normal saline and fixed in 10% formalin for 2 days followed with bovine solution for 6 h. Then the livers were paraffin embedded and 5 µ thickness microtone sections were made.[33] The sections were processed in alcohol-xylene series and stained with haematoxylin and eosin. The slides were studied under a light micro-scope for any histological damage/protection.

h) Statistical Analysis

The data are represented as mean ± S.E.M. Students't-test is used for statistical analysis of blood serum parameters and for statistical analysis of liver enzymes

III. Results

The acute oral toxicity study of *Melia azedarach* Linn, *Catharanthus Rosea* and *Brassica oleracea L.var.capitata* showed no mortality upto 2000 mg/kg.The effect of ethanol extracts of *Melia azedarach* Linn, *Catharanthus Rosea* and *Brassica oleracea L.var.capitata* on serum transaminases, alkaline phosphates, bilirubin and total protein level in Simvastatin intoxicated rats are summarized in Table 1. There was a significant increase in bilirubin levels, SGPT, SGOT and ALP, in Simvastatin intoxicated group(Group II) compared to the normal control group(Group I), while the total protein levels were significantly decreased from the level of 6.46 g/dl to 3.31g/dl in Simvastatin intoxicated rats. Extracts treatment groups such as Group III to Group VIII and standerd group such as Group IX (Simvastatin 20mg/kg.p.o + Silymarin 25mg/kg, p.o) showed significantly decreased the elevated serum marker enzymes when given orally and reversed the altered total protein to almost normal level (Table 1).

From the above results (Table1), it shows that ethanolic extracts of ***Melia azedarach*** and *Brassica oleracea L. var. Capitata* (300mg/kg, and 500mg/kg,) are more effiective than ***Catharanthus roseus*** (300mg/kg, and 500mg/kg,) of which *Brassica oleracea L. var* (500mg/kg,) is shown to be more effective than ***Melia azedarach*** (500mg/kg,) in restoration of the above parameters to normal level.

Table 1 : Effect of various groups on some serum chemical parameters

Groups	SGPT levels (U/L)	SGOT levels (U/L)	ALP levels (U/L)	Total bilirubin (mg/dl)	Total protein(g/dl)
Group I	34.32±0.75	36.89±2.30	71.45 ± 0.22	0.40±0.02	6.46±0.02
Group II	126.9±1.50[a, **]	179.95±1.350[a, **]	172.68±0.64[a, **]	1.96±0.12[a,**]	3.31±0.08[a,**]
Group I11	83.2±0.27[b,**]	123.56±0.750[b,**]	133.0±1.63[b,**]	0.68±0.08[b,**]	4.08±0.15[b,**]
Group IV	46.6±0.55[b,**]	68.63±0.82[b, **]	98.0±1.24[b,**]	0.56±0.01[b,**]	6.12±0.15[b,**]
Group V	112.2±0.60[b,*]	168.01±2.75[b,*]	162.2±2.42[b,*]	1.42±0.03[b,*]	3.98±0.06[b,*]
Group VI	98.6±2.38[b,**]	142.58 ±2.53[b,**]	118.24±1.88[b, **]	0.99±0.05[b,**]	4.41±0.02[b,**]
Group VII	48.6±1.62[b,**]	70.23±1.34[b,**]	93.6±0.53**	0.58±0.06[b,**]	5.45±0.08[b,**]
Group VIII	38.23±1.42[b, **]	39.09±1.60[b,**]	74.3±1.72***	0.45±0.04[b,**]	6.24±0.07[b,**]
Group IX	36.98±2.74[b, **]	38.67±1.25[b,**]	72.6±1.04[b,**]	0.42±0.02[b,**]	6.50±0.12[b,**]

Values are mean ± SEM (n=6) one way ANOVA followed by Dunnet's't' multiple Comparison test. a - Group I vs. Group II; b – Group II vs. Group III to Group IX; Where, * represents significant at <0.05,

** represents highly significant at p< 0.01, and
*** represents very significant at p<0.001. All values are compared with toxicant

Histopathology of the liver of various groups:

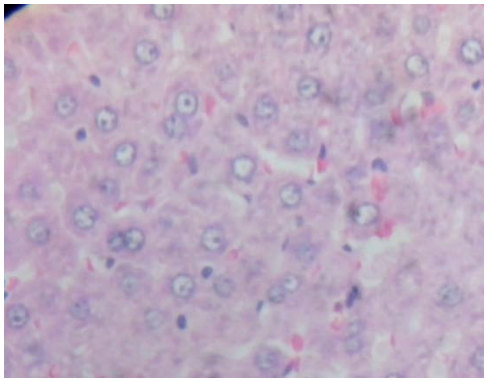

Fig. 1 : Group I

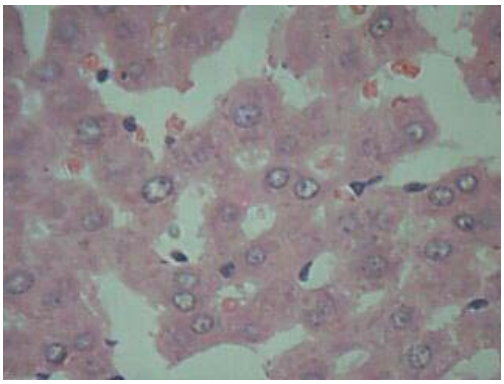

Fig. 2 : Group II

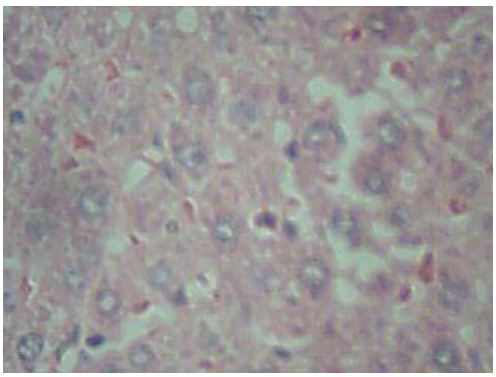

Fig. 3 : Group III

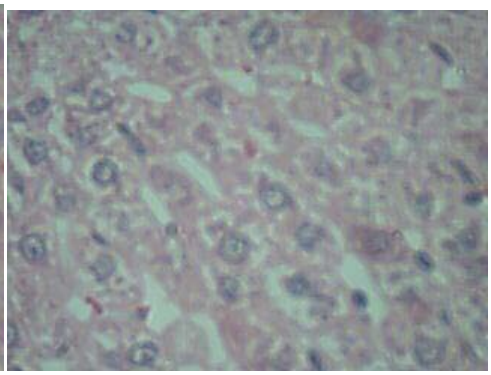

Fig. 4 : Group IV

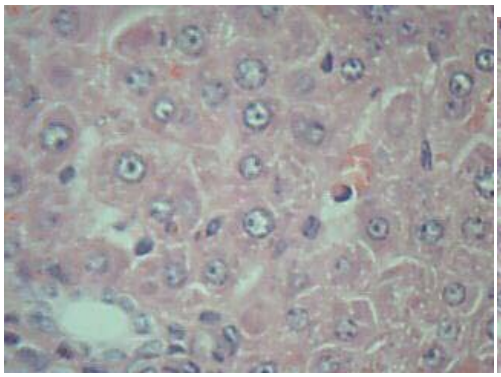

Fig. 5 : Group V

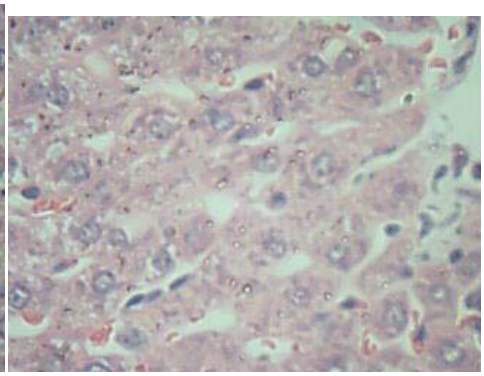

Fig. 6 : Group VI

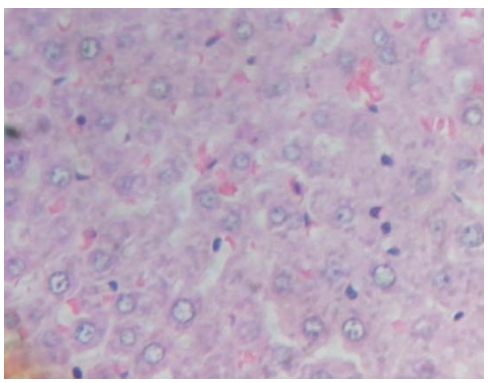

Fig. 7 : Group VII

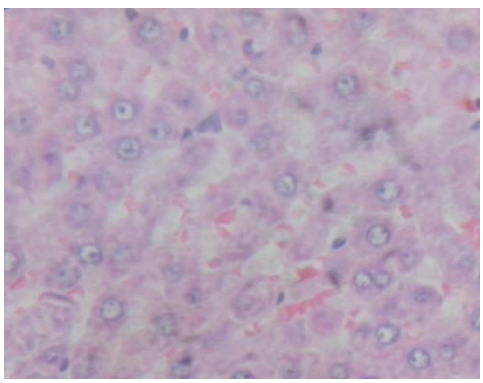

Fig. 8 : Group VIII

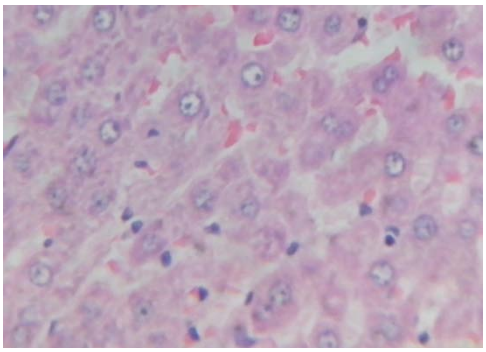

Fig. 9 : Group IX

IV. Discussion

The liver is a vital organ present in vertebrates and some other animals. The liver can be injured by many chemicals and drugs.[34] It is reported that more than 900 drugs have been implicated in causing liver injury [2] and it is the most common reason for a drug to be withdrawn from the market. Drug induced liver injury is responsible for 5% of all hospital admissions and 50% of all acute liver failures.[3, 4]. Statins are now among the most frequently prescribed medications and are currently used by about 25 million people worldwide. During hepatic damage, cellular enzyme like SGOT, SGPT, ALP and serum bilirubin present in the liver cell, leak into the serum resulting to increase in concentration. [35]

In the previous study, it was reported that simvastatin caused oxidative stress mediated hepatotoxicity.[36] The most common clinical hepatic manifestation of statins is asymptomatic elevation in aminotransferases.[37-40] Elevations to.3 times upper limit of normal occur in 1% to 3%.[41]

In the present study, it shows that ethanolic extracts of *Melia azedarach* Linn, *Catharanthus Rosea* and *Brassica oleracea L.var.capitata* significantly decreased the elevated serum marker enzymes and reversed the altered total protein to almost normal level. *Brassica oleracea L.var.capitata*(500mg/kg,) is shown to be more effective than ***Melia azedarach*** (500mg/kg,) *and Catharanthus Rosea* (500mg/kg,) while *Catharanthus Rosea* shows moderate activity than other extracts.It is reported that phenols are responsible for the variation in the antioxidant activity of the plant .[42] They exhibit antioxidant activity by inactivating lipid free radicals or preventing decomposition of hydroperoxides into free radicals. [43, 44] Phenolic compounds are considered to be the most important antioxidative components of herbs and other plant materials. [45, 46]

Histological changes such as fatty changes in hepatocytes (steatosis) and perivenular fibrosis were observed in simvastatin intoxicated group. Ethanolic extracts of *Melia azedarach* Linn, *Catharanthus Rosea* and *Brassica oleracea L.var.capitata* (300 mg/kg and 500mg/kg, p.o) significantly prevented these histological changes, further indicating their hepatoprotective activity. Although there is insufficient information to establish the mechanism of action of *Melia azedarach*,protection, this could be due to its antioxidant property of the phenolic compounds.

V. Conclusion

In conclusion, the results of present study demonstrate that *Melia azedarach* and *Brassica oleracea L.var.capitata* leaves extracts (300 mg/kg and 500mg/kg,) has potent hepatoprotective activity than *Catharanthus Rosea,* against simvastatin induced liver damage. Our study also implies that the hepatoprotective effects of *Melia azedarach* Linn, *Catharanthus Rosea* and *Brassica oleracea L.var.capitata* may be due to its antioxidant property of the phenolic compounds. Further investigation is in progress to determine the exact phytoconstituents responsible for hepataprotective effect.

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Medicinal Plants with Antifertility Activity-An Overview

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Abstract - Medicinal plants, is a common word which can utter in every one's mouth that are helpful in treating many diseases which can't be done by even allopathic medicine. Among those the birth control and at the same time increasing the fertility in human beings are both become major problems now a days. This review presents updated information gathered on scientifically proved medicinal plants used for anti-fertility activity. This study provides the information on botanical name, family, parts used, solvents used and their chemical constituents present in plants. In spite of rapid progress and spread of modern medicine and surgery, faith in and popularity of traditional methods has not decreased. There are a large number of studies which supports the anti-fertility effects of traditional herbal medicines. The aim of this review is to highlight the work on anti-fertility of plant origin. The present paper also involves various plant drugs and their bioactive extracts involved in anti-fertility mechanism. This article may help investigators to identify medicinal plants responsible for anti-fertility activity.

Keywords : *herbal medicines, anti-fertility plants.*

GJMR-B Classification : *NLMC Code: WP 570*

Strictly as per the compliance and regulations of:

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Keywords : herbal medicines, anti-fertility plants.

I. Introduction

Ethanobotany is the new branch which deals the medicinal plants and their activities. The applications of this field are enormous in regular life. Controlling the birth rate in India is the major problem; at the same time some parents are unable to have babies, for that they are preferring fertility centers. To cope these two types of problems now natural medicine took the time to emphasize without technical apparatus involvement the birth may control through contraception (herbal contraception) and also can have babies through natural medicine intake.

There are several other articles, journals and references which have been discussed about the antifertility and profertility individually. But this review article shows the both sections including some pharmacological activities. In 2005 G.C., world population is estimated to be 6.5 billion. This number is expected to increase by 2.5 billion over the next 45 years, 6.5 billion to 9.1 billion in 2050. Today, 95 per cent of all population growth is absorbed by the developing world and 5 per cent by the developed world. In the case of Ethiopia total population is estimated to be 74.2 million in 2005 with current growth rate of 2.9 per cent per year. The average birth per woman is 6.14 and the contraceptive prevalence is 8.1 percent [1].

Moreover major population of the country lives in rural areas and those people have not approach to the modern methods of family planning. Traditional sterilization method based on herbal medicines is used to control population growth rate; including abortion at initial weeks, preventing conception or making the either member of the couple sterile. Perusal of literature revealed that enough work has been done on different medicinal aspects of plants of this area except for gynaecological disorders, abortifacient herbals and plants used to induce abortion [2-4].

Several plant products inhibit male and female fertility and may be developed into contraceptives. Even though, many indigenous plants have been shown to prevent the birth, only few plants have so far been investigated for anti-fertility activity. The World Health Organization (WHO) has set up a Task Force on Plant Research for fertility regulation with an objective to find new orally active non-steroidal contraceptive compounds. Various medicinal plant extracts have been tested for their anti-fertility activity both in male and female.

Some of these plants had spermicidal and altered hormone levels. It is necessary to use biologically active botanical substances or fertility-regulating agents of plant origin which are eco-friendly effects [5,6].

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Table 1 : List of Anti-fertility plants

Botanical name	Family	Parts used	Chemical constituents	References
Abrus precatonius Linn	Fabaceae	Whole plant	Alkaloids, steroids, fixed oils, anthocyannins	Abu et al [7]
Acacia leucophploea Roxb	Fabaceae	Roots	Tannins, phenols, proteins	Dheeraj ahirwar [8]
Aegle marmelos Linn	Rutaceae	Leaves	Alkaloids, terpenes, steroids	Satheesh et al [9]
Butea monosperma Lam	Fabaceae	Whole plant	Stigmosterol flavonoids, amino acids	Ashish mishra et al [10]
Careya arborea Roxb	Lecythidaceae	Roots	Phyto-estrogens, Sito-sterol	A.K.haloi et al [11]
Cissampelos pareira Linn	Manispermaceae	Whole plant	Alkaloids, chalconeflavone	Samanthajhuma et al [12]
Citrus medica Linn	Rutaceae	Fruit peel	Citroflavanoids, glucosides, triterpenoids	Monica kachroo et al [13]
Curcuma longa Linn	Zingiberaceae	Rhizomes	Curcumin Flavonoids	Amit kumar ghosh et al [14]
Dodonea viscosa Linn	Sapindaceae	Whole plant	Alkaloids, phytosterols, poly phenols	R.ramya et al [15]
Hymenocardia acida Tul	Euphorbiaceae	Stem bark	Triterpenoids, glycosides	Abu et al [16]
Madhuca indica Linn	Sapotaceae	Leaves	Triterpenoids	Shivabasavaiah et al [17]
Ocimum gratissimum Linn	Caesalpiniaceae	Stems	Anthraquinones, flavanoids,	Yuvaraj et al [18]
Plumbago rosea Linn	Plumbasinaceae	Leaves	Sitosterol glycosides, tannins, fatty alcohol	Sheeja et al [19]
Raphanus sativus Linn	Brassicaceae	Roots	Raphan alkaloids	Mishra et al [20]
Tabernaemontana divaricata Linn	Apocynaceae	Flowers	Steroids, tannins Flavanoids, aminoacids	Mohd.azeemuddin nukhram et al [21]
Trachysperm ammi Linn	Umbelliferae	Fruits	Tannins, saponins, flavonoids, glycosides	Surendra kumar et al [22]
Tragia involucrata Linn	Euphorbiaceae	Aerial parts	Flavonoids, terpenoids	Chandrashekhar et al [23]

II. Conclusion

Finally, it was clear that the medicinal plants play an important role in treating various diseases. The herbal plants and their extracts have significant anti-fertility activity in animal models. This review showed that above-mentioned medicinal plants possess anti-fertility activity on dose dependent manner and can be used as an alternative for oral contraceptives which are currently in use for birth control.

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1. Choosing the topic: In most cases, the topic is searched by the interest of author but it can be also suggested by the guides. You can have several topics and then you can judge that in which topic or subject you are finding yourself most comfortable. This can be done by asking several questions to yourself, like Will I be able to carry our search in this area? Will I find all necessary recourses to accomplish the search? Will I be able to find all information in this field area? If the answer of these types of questions will be "Yes" then you can choose that topic. In most of the cases, you may have to conduct the surveys and have to visit several places because this field is related to Computer Science and Information Technology. Also, you may have to do a lot of work to find all rise and falls regarding the various data of that subject. Sometimes, detailed information plays a vital role, instead of short information.

2. Evaluators are human: First thing to remember that evaluators are also human being. They are not only meant for rejecting a paper. They are here to evaluate your paper. So, present your Best.

3. Think Like Evaluators: If you are in a confusion or getting demotivated that your paper will be accepted by evaluators or not, then think and try to evaluate your paper like an Evaluator. Try to understand that what an evaluator wants in your research paper and automatically you will have your answer.

4. Make blueprints of paper: The outline is the plan or framework that will help you to arrange your thoughts. It will make your paper logical. But remember that all points of your outline must be related to the topic you have chosen.

5. Ask your Guides: If you are having any difficulty in your research, then do not hesitate to share your difficulty to your guide (if you have any). They will surely help you out and resolve your doubts. If you can't clarify what exactly you require for your work then ask the supervisor to help you with the alternative. He might also provide you the list of essential readings.

6. Use of computer is recommended: As you are doing research in the field of Computer Science, then this point is quite obvious.

7. Use right software: Always use good quality software packages. If you are not capable to judge good software then you can lose quality of your paper unknowingly. There are various software programs available to help you, which you can get through Internet.

8. Use the Internet for help: An excellent start for your paper can be by using the Google. It is an excellent search engine, where you can have your doubts resolved. You may also read some answers for the frequent question how to write my research paper or find model research paper. From the internet library you can download books. If you have all required books make important reading selecting and analyzing the specified information. Then put together research paper sketch out.

9. Use and get big pictures: Always use encyclopedias, Wikipedia to get pictures so that you can go into the depth.

10. Bookmarks are useful: When you read any book or magazine, you generally use bookmarks, right! It is a good habit, which helps to not to lose your continuity. You should always use bookmarks while searching on Internet also, which will make your search easier.

11. Revise what you wrote: When you write anything, always read it, summarize it and then finalize it.

12. Make all efforts: Make all efforts to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in introduction, that what is the need of a particular research paper. Polish your work by good skill of writing and always give an evaluator, what he wants.

13. Have backups: When you are going to do any important thing like making research paper, you should always have backup copies of it either in your computer or in paper. This will help you to not to lose any of your important.

14. Produce good diagrams of your own: Always try to include good charts or diagrams in your paper to improve quality. Using several and unnecessary diagrams will degrade the quality of your paper by creating "hotchpotch." So always, try to make and include those diagrams, which are made by your own to improve readability and understandability of your paper.

15. Use of direct quotes: When you do research relevant to literature, history or current affairs then use of quotes become essential but if study is relevant to science then use of quotes is not preferable.

16. Use proper verb tense: Use proper verb tenses in your paper. Use past tense, to present those events that happened. Use present tense to indicate events that are going on. Use future tense to indicate future happening events. Use of improper and wrong tenses will confuse the evaluator. Avoid the sentences that are incomplete.

17. Never use online paper: If you are getting any paper on Internet, then never use it as your research paper because it might be possible that evaluator has already seen it or maybe it is outdated version.

18. Pick a good study spot: To do your research studies always try to pick a spot, which is quiet. Every spot is not for studies. Spot that suits you choose it and proceed further.

19. Know what you know: Always try to know, what you know by making objectives. Else, you will be confused and cannot achieve your target.

20. Use good quality grammar: Always use a good quality grammar and use words that will throw positive impact on evaluator. Use of good quality grammar does not mean to use tough words, that for each word the evaluator has to go through dictionary. Do not start sentence with a conjunction. Do not fragment sentences. Eliminate one-word sentences. Ignore passive voice. Do not ever use a big word when a diminutive one would suffice. Verbs have to be in agreement with their subjects. Prepositions are not expressions to finish sentences with. It is incorrect to ever divide an infinitive. Avoid clichés like the disease. Also, always shun irritating alliteration. Use language that is simple and straight forward. put together a neat summary.

21. Arrangement of information: Each section of the main body should start with an opening sentence and there should be a changeover at the end of the section. Give only valid and powerful arguments to your topic. You may also maintain your arguments with records.

22. Never start in last minute: Always start at right time and give enough time to research work. Leaving everything to the last minute will degrade your paper and spoil your work.

23. Multitasking in research is not good: Doing several things at the same time proves bad habit in case of research activity. Research is an area, where everything has a particular time slot. Divide your research work in parts and do particular part in particular time slot.

24. Never copy others' work: Never copy others' work and give it your name because if evaluator has seen it anywhere you will be in trouble.

25. Take proper rest and food: No matter how many hours you spend for your research activity, if you are not taking care of your health then all your efforts will be in vain. For a quality research, study is must, and this can be done by taking proper rest and food.

26. Go for seminars: Attend seminars if the topic is relevant to your research area. Utilize all your resources.

27. Refresh your mind after intervals: Try to give rest to your mind by listening to soft music or by sleeping in intervals. This will also improve your memory.

28. Make colleagues: Always try to make colleagues. No matter how sharper or intelligent you are, if you make colleagues you can have several ideas, which will be helpful for your research.

29. Think technically: Always think technically. If anything happens, then search its reasons, its benefits, and demerits.

30. Think and then print: When you will go to print your paper, notice that tables are not be split, headings are not detached from their descriptions, and page sequence is maintained.

31. Adding unnecessary information: Do not add unnecessary information, like, I have used MS Excel to draw graph. Do not add irrelevant and inappropriate material. These all will create superfluous. Foreign terminology and phrases are not apropos. One should NEVER take a broad view. Analogy in script is like feathers on a snake. Not at all use a large word when a very small one would be sufficient. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Amplification is a billion times of inferior quality than sarcasm.

32. Never oversimplify everything: To add material in your research paper, never go for oversimplification. This will definitely irritate the evaluator. Be more or less specific. Also too, by no means, ever use rhythmic redundancies. Contractions aren't essential and shouldn't be there used. Comparisons are as terrible as clichés. Give up ampersands and abbreviations, and so on. Remove commas, that are, not necessary. Parenthetical words however should be together with this in commas. Understatement is all the time the complete best way to put onward earth-shaking thoughts. Give a detailed literary review.

33. Report concluded results: Use concluded results. From raw data, filter the results and then conclude your studies based on measurements and observations taken. Significant figures and appropriate number of decimal places should be used. Parenthetical remarks are prohibitive. Proofread carefully at final stage. In the end give outline to your arguments. Spot out perspectives of further study of this subject. Justify your conclusion by at the bottom of them with sufficient justifications and examples.

34. After conclusion: Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium though which your research is going to be in print to the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects in your research.

Informal Guidelines of Research Paper Writing

Key points to remember:

- Submit all work in its final form.
- Write your paper in the form, which is presented in the guidelines using the template.
- Please note the criterion for grading the final paper by peer-reviewers.

Final Points:

A purpose of organizing a research paper is to let people to interpret your effort selectively. The journal requires the following sections, submitted in the order listed, each section to start on a new page.

The introduction will be compiled from reference matter and will reflect the design processes or outline of basis that direct you to make study. As you will carry out the process of study, the method and process section will be constructed as like that. The result segment will show related statistics in nearly sequential order and will direct the reviewers next to the similar intellectual paths throughout the data that you took to carry out your study. The discussion section will provide understanding of the data and projections as to the implication of the results. The use of good quality references all through the paper will give the effort trustworthiness by representing an alertness of prior workings.

Writing a research paper is not an easy job no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record keeping are the only means to make straightforward the progression.

General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

To make a paper clear

· Adhere to recommended page limits

Mistakes to evade

- Insertion a title at the foot of a page with the subsequent text on the next page
- Separating a table/chart or figure - impound each figure/table to a single page
- Submitting a manuscript with pages out of sequence

In every sections of your document

· Use standard writing style including articles ("a", "the," etc.)

· Keep on paying attention on the research topic of the paper

· Use paragraphs to split each significant point (excluding for the abstract)

· Align the primary line of each section

· Present your points in sound order

· Use present tense to report well accepted

· Use past tense to describe specific results

· Shun familiar wording, don't address the reviewer directly, and don't use slang, slang language, or superlatives

· Shun use of extra pictures - include only those figures essential to presenting results

Title Page:

Choose a revealing title. It should be short. It should not have non-standard acronyms or abbreviations. It should not exceed two printed lines. It should include the name(s) and address (es) of all authors.

Abstract:

The summary should be two hundred words or less. It should briefly and clearly explain the key findings reported in the manuscript--must have precise statistics. It should not have abnormal acronyms or abbreviations. It should be logical in itself. Shun citing references at this point.

An abstract is a brief distinct paragraph summary of finished work or work in development. In a minute or less a reviewer can be taught the foundation behind the study, common approach to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Yet, use comprehensive sentences and do not let go readability for briefness. You can maintain it succinct by phrasing sentences so that they provide more than lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study, with the subsequent elements in any summary. Try to maintain the initial two items to no more than one ruling each.

- Reason of the study - theory, overall issue, purpose
- Fundamental goal
- To the point depiction of the research
- Consequences, including definite statistics - if the consequences are quantitative in nature, account quantitative data; results of any numerical analysis should be reported
- Significant conclusions or questions that track from the research(es)

Approach:

- Single section, and succinct
- As a outline of job done, it is always written in past tense
- A conceptual should situate on its own, and not submit to any other part of the paper such as a form or table
- Center on shortening results - bound background information to a verdict or two, if completely necessary
- What you account in an conceptual must be regular with what you reported in the manuscript
- Exact spelling, clearness of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else

Introduction:

The **Introduction** should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable to comprehend and calculate the purpose of your study without having to submit to other works. The basis for the study should be offered. Give most important references but shun difficult to make a comprehensive appraisal of the topic. In the introduction, describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will have no attention in your result. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here. Following approach can create a valuable beginning:

- Explain the value (significance) of the study
- Shield the model - why did you employ this particular system or method? What is its compensation? You strength remark on its appropriateness from a abstract point of vision as well as point out sensible reasons for using it.
- Present a justification. Status your particular theory (es) or aim(s), and describe the logic that led you to choose them.
- Very for a short time explain the tentative propose and how it skilled the declared objectives.

Approach:

- Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done.
- Sort out your thoughts; manufacture one key point with every section. If you make the four points listed above, you will need a least of four paragraphs.

- Present surroundings information only as desirable in order hold up a situation. The reviewer does not desire to read the whole thing you know about a topic.
- Shape the theory/purpose specifically - do not take a broad view.
- As always, give awareness to spelling, simplicity and correctness of sentences and phrases.

Procedures (Methods and Materials):

This part is supposed to be the easiest to carve if you have good skills. A sound written Procedures segment allows a capable scientist to replacement your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt for the least amount of information that would permit another capable scientist to spare your outcome but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section. When a technique is used that has been well described in another object, mention the specific item describing a way but draw the basic principle while stating the situation. The purpose is to text all particular resources and broad procedures, so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step by step report of the whole thing you did, nor is a methods section a set of orders.

Materials:

- Explain materials individually only if the study is so complex that it saves liberty this way.
- Embrace particular materials, and any tools or provisions that are not frequently found in laboratories.
- Do not take in frequently found.
- If use of a definite type of tools.
- Materials may be reported in a part section or else they may be recognized along with your measures.

Methods:

- Report the method (not particulars of each process that engaged the same methodology)
- Describe the method entirely
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures
- Simplify - details how procedures were completed not how they were exclusively performed on a particular day.
- If well known procedures were used, account the procedure by name, possibly with reference, and that's all.

Approach:

- It is embarrassed or not possible to use vigorous voice when documenting methods with no using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result when script up the methods most authors use third person passive voice.
- Use standard style in this and in every other part of the paper - avoid familiar lists, and use full sentences.

What to keep away from

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings - save it for the argument.
- Leave out information that is immaterial to a third party.

Results:

The principle of a results segment is to present and demonstrate your conclusion. Create this part a entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Carry on to be to the point, by means of statistics and tables, if suitable, to present consequences most efficiently.You must obviously differentiate material that would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matter should not be submitted at all except requested by the instructor.

Content

- Sum up your conclusion in text and demonstrate them, if suitable, with figures and tables.
- In manuscript, explain each of your consequences, point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation an exacting study.
- Explain results of control experiments and comprise remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or in manuscript form.

What to stay away from

- Do not discuss or infer your outcome, report surroundings information, or try to explain anything.
- Not at all, take in raw data or intermediate calculations in a research manuscript.
- Do not present the similar data more than once.
- Manuscript should complement any figures or tables, not duplicate the identical information.
- Never confuse figures with tables - there is a difference.

Approach

- As forever, use past tense when you submit to your results, and put the whole thing in a reasonable order.
- Put figures and tables, appropriately numbered, in order at the end of the report
- If you desire, you may place your figures and tables properly within the text of your results part.

Figures and tables

- If you put figures and tables at the end of the details, make certain that they are visibly distinguished from any attach appendix materials, such as raw facts
- Despite of position, each figure must be numbered one after the other and complete with subtitle
- In spite of position, each table must be titled, numbered one after the other and complete with heading
- All figure and table must be adequately complete that it could situate on its own, divide from text

Discussion:

The Discussion is expected the trickiest segment to write and describe. A lot of papers submitted for journal are discarded based on problems with the Discussion. There is no head of state for how long a argument should be. Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implication of the study. The purpose here is to offer an understanding of your results and hold up for all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of result should be visibly described. Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved with prospect, and let it drop at that.

- Make a decision if each premise is supported, discarded, or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."
- Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work
- You may propose future guidelines, such as how the experiment might be personalized to accomplish a new idea.
- Give details all of your remarks as much as possible, focus on mechanisms.
- Make a decision if the tentative design sufficiently addressed the theory, and whether or not it was correctly restricted.
- Try to present substitute explanations if sensible alternatives be present.
- One research will not counter an overall question, so maintain the large picture in mind, where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

Approach:

- When you refer to information, differentiate data generated by your own studies from available information
- Submit to work done by specific persons (including you) in past tense.
- Submit to generally acknowledged facts and main beliefs in present tense.

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- To guard yourself and others from possible illegal use please do not permit anyone right to use to your paper and files.

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Topics	Grades		
	A-B	**C-D**	**E-F**
Abstract	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
Introduction	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
Methods and Procedures	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
Result	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
Discussion	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
References	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring

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