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FORMULATION AND EVALUATION OF GLIMEPIRIDEFLOATING MICROSPHERES

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ABSTRACT

The objective of the present study was to develop Glimepiride floating microspheres in order to achieve an extended retention in the upper GIT, which enhances the absorption and improves the bioavailability. The microspheres were prepared by emulsion solvent diffusion-evaporation method using different ratios of rate controlling polymers ethyl cellulose and hydroxy propyl methyl cellulose, Glimepirideis used in each formulation at constant ratio. The mixture of dichloromethane and ethanol at ratio of (1:1), with tween 80 as the surfactant. The prepared microspheres were evaluated for percentage yield, particle size, entrapment efficiency, shape and surface characterization, buoyancy, in vitro dissolution studies and drug release mechanismwas interpretated by kinetic model. The effect of polymer concentration on these parameters was investigated. The studies revealed that increase in concentration of hydrophilic polymer (HPMC) increased the drug release from the floating microspheres. The formulation F9 (Glimepiride: HPMC:EC is 1:3:2) was selected as best formulation, and it follows zero order drug release with 86.63% entrapment efficiency, 98.16% drug content, 90% buoyancy, 87.48%*In-vitro* drug release at 12^{th} hour.

INTRODUCTION

Oral medication conveyance is the most generally utilized course of organization amongevery one of the courses that have been investigated for foundational conveyance of medicationsthrough pharmaceutical results of various measurement structure. Oral course is viewed as mostprominent, helpful and safe because of simplicity of organization, quiet acknowledgment, and savvyassembling process. (1)

The greater part of the pharmaceutical items intended for oral conveyance are traditional medication conveyance frameworks. Issue experienced with ordinary measurements structures are: drugs with short half-life require visit organization, which may expand shot of missing portion of medication prompting poor patient consistence.

So as to defeat the disadvantages of regular medication conveyance framework, a few specializedprogressionshave prompted advancement of controlled medication conveyance framework that could reform strategy forprescription and give various remedial advantages.[4]

MATERIALS & INSTRUMENTS

MATERIALS USED

S.NO	INGREDIANTS ANDREAGENTS	MANUFACTURER AND SUPPLIER
1	Glimepiride	Med rich Pvt. Ltd
2	Ethylcellulose N10	Loba chemie pvt.ltd, Mumbai.
3	Hydroxypropyl methyl celluloseK100M	Loba chemie pvt.ltd, Mumbai.
4	Dichloromethane	Med rich Pvt. Ltd
5	Ethanol	Med rich Pvt. Ltd
6	Tween 80	Loba chemie pvt.ltd, Mumbai

INSTRUMENTS USED

S.NO	INSTRUMENTS	COMPANY
1	Digital balance	Shimadzu ELB 300
2	Probe sonificator	Elektro craft India Pvt.Ltd, Mumbai.
3	Orbitek shaker	Orbitek shaker, chenni.
4	Dissolution apparatus USP XXIII	Veego tablet dissolution apparatus, Chennai
5	Double beam UV spectrophotometer	Perkin Elmer Lambda-25 UV/VIS spectrometer.

METHODOLOGYPREFORMULATION STUDIES

Before formulation of drug substance in to dosage form, it is essential that drug andpolymer should be chemically and physically characterized. Preformulation studies give the information needed to define thenature of drug

substance and provide a frame work for a drug combination with pharmaceutical excipientsin the fabrication ofa dosage form.

CONSTRUCTION OF STANDARD CURVE FOR GLIMEPIRIDE

Glimepiride can be estimated spectrophotometrically at 224 nm as it obeys Beer's-Lambert's lawlimit is the range of5-25 µg/ml.

Preparation of reagents Preparation of 0.1 N HCl:

Dissolve 8.5 mlofconcentrated HCl in 1000 ml ofdistilled water.

Preparation of standard drug solutionStock solution:

100 mg of Glimepiride was dissolved in 100 ml of 0.1 N HCl, to get a solution of1000 µg/ml concentration.

Standard solution

10 ml of stock solution was made to 100 ml with 0.1 N HCl thus giving a concentration of100 µg/ml. Aliquot of standard drug solution ranging from 0.5 ml, 1 ml,1.5 ml, 2 ml and 2.5 ml were transferred into10 ml volumetric flask and were diluted up to the mark with 0.1 N HCl. Thus, the final concentrationranges from 5-25 µg/ml. Absorbance of each solution was measured at 224 nm against 0.1 N HCl as a blank. Aplot ofconcentrations ofdrug versus absorbance was plotted.

The linear regression analysis was done on absorbance data points. A straight-lineequationwas generatedto facilitate the calculation ofamount ofdrug.

The equation is as follows:

$$Y = mx + c$$

Where **Y** = Absorbance, m = Slope, x =Concentration, c = Intercept.

Calculation of controlled release dose [53]

Required dose = conventionaldose $(1+0.693 \times \tau/t_{1/2})$Where as,

τ = Duration ofdose

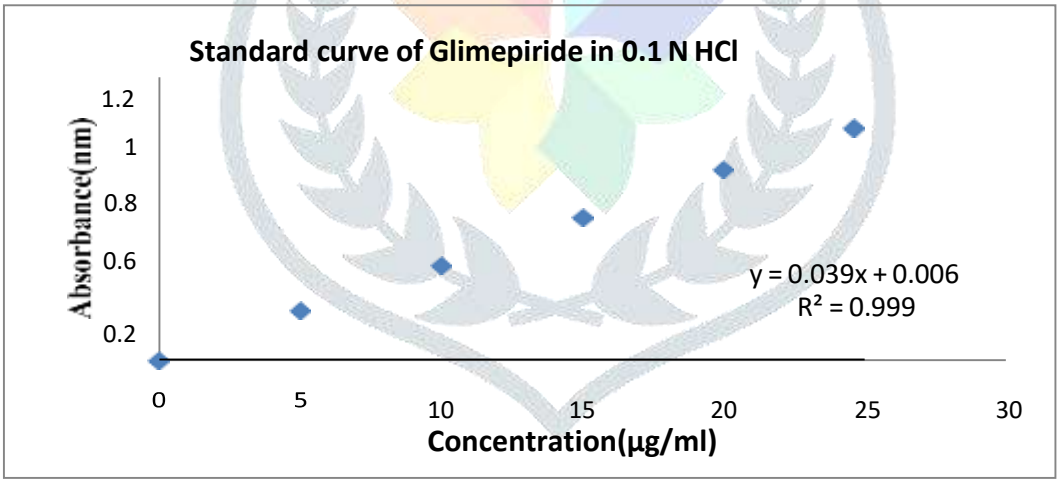
t = Half-life ofdrugRequired dose = 4 (1+0.693 × 12/5)Required dose = 10mg ofGlimepiride

CONSTRUCTION OF STANDARD CURVE FOR GLIMEPIRIDE

Standard curve for Glimepiride

S.NO	Concentration in µg/ml	Absorbance at 224 nm
1	5.00	0.210
2	10.00	0.401
3	15.00	0.606
4	20.00	0.810
5	25.00	0.988
Slope		0.039
Correlation coefficient		0.999

STANDARD CURVE FOR GLIMEPIRIDE IN 0.1 N HCl



DATA FOR PARTICLE SIZE OF GLIMEPIRIDE FLOATING MICROSPHERES

FORMULATION CODE	MEAN PARTICLE SIZE (µm)
F1	114±1.309
F2	127±1.563
F3	157±2.039
F4	139±1.875
F5	168±0.935
F6	198±2.745
F7	174±1.648
F8	217±1.178
F9	247±1.825
F10	235±2.148
F11	253±3.053
F12	265±1.509

*Each value represents the mean±S.D. ofthree experiments

DATA FOR PERCENTAGE DRUG CONTENT OFGLIMIPIRIDEFLOATINGMICROSPHERES

FORMULATION CODE	PERCENTAGE DRUG CONTENTOF MICROSPHERES
F1	70.56±2.274
F2	71.92±1.932
F3	74.69±0.615
F4	75.71±0.991
F5	78.36±3.846
F6	81.95±1.562
F7	79.21±2.428
F8	84.83±1.541
F9	98.16±1.357
F10	88.15±1.864
F11	96.24±1.649
F12	94.57±1.162

*Each value represents the mean±S.D. ofthree experiments

DATA FOR PERCENTAGE YIELD OF GLIMIPIRIDE FLOATINGMICROSPHERES

FORMULATION CODE	PERCENTAGE YIELDOF MICROSPHERES
F1	61±1.862
F2	64±2.517
F3	67±1.953
F4	66±1.325
F5	69±1.472
F6	72±2.951
F7	70±1.645
F8	74±2.153
F9	77±1.226
F10	75±2.184
F11	79±1.025
F12	81±1.951

*Each value represents the mean±S.D. ofthree experiments

DATA FOR PERCENTAGE DRUG ENTRAPMENT EFFICIENCY OFGLIMEPIRIDE FLOATING MICROSPHERES

Formulation code	Theoretical drug contentin %	Practical drugcontentin %	Entrapment efficiency in %
F1	15.25	9.83	64.45±2.186
F2	12.92	8.61	66.64±3.017
F3	9.45	6.97	73.75±1.053
F4	12.92	9.36	72.44±2.38
F5	9.45	7.17	75.87±1.462
F6	8.15	6.45	79.14±1.954
F7	9.45	7.29	77.14±1.171
F8	8.15	6.54	80.24±1.436
F9	7.26	6.29	86.63±1.245
F10	8.15	6.73	82.57±1.325
F11	7.26	6.32	87.05±1.168
F12	6.02	5.38	89.36±2.428

*Each value represents the mean±S.D. ofthree experiments

DATA FOR IN VITRO EVALUATION OF FLOATING ABILITY FORGLIMEPIRIDE FLOATING MICROSPHERES

FORMULATION CODE	BUOYANCY PERCENTAGE
F1	70±1.957
F2	71±1.436
F3	79±2.049
F4	74±1.875
F5	76±2.745
F6	82±1.358
F7	80±1.594
F8	84±2.215
F9	90±1.259
F10	87±1.427
F11	91±1.052
F12	94±1.314

*Each value represents the mean±S.D. ofthree experiments

DATA FOR *INVITRO* DRUG RELEASE OF GLIMEPIRIDE FLOATINGMICROSPHERES

***In-Vitro* Drug release of Formulation F1**

Time (hrs)	Absorbance (nm)	Concentration µg/ml	Amount of drug release	Cum % of drug release
0	0	0	0	0
1	0.014	0.374	3.37	16.86±1.170
2	0.022	0.562	5.06	25.32±3.716
3	0.030	0.770	6.93	34.65±1.709
4	0.037	0.944	8.5	42.52±2.128
5	0.043	1.094	9.84	49.23±1.053
6	0.050	1.274	11.47	57.37±1.569
7	0.056	1.421	12.79	63.96±2.52
8	0.062	1.556	14	70.02±1.357
9	0.068	1.723	15.5	77.54±1.214
10	0.072	1.816	16.34	81.73±1.354
11	0.076	1.919	17.27	86.37±2.341
12	0.081	2.046	18.41	92.07±1.368

*Each value represents the mean±S.D. ofthree experiments

In- Vitro Drug release of Formulation F2

Time (hrs)	Absorbance (nm)	Concentration µg/ml	Amount of drug release	Cum % of drugrelease
0	0	0	0	0
1	0.022	0.574	5.168	25.84±1.894
2	0.028	0.716	6.452	32.26±1.247
3	0.035	0.887	7.984	39.92±1.432
4	0.043	1.095	9.856	49.28±2.169
5	0.049	1.245	11.21	56.05±1.689
6	0.059	1.494	13.45	67.27±1.715
7	0.066	1.656	14.9	74.53±1.357
8	0.071	1.782	16.03	80.19±1.364
9	0.084	2.105	18.94	94.73±2.048

*Each value represents the mean±S.D. ofthree experiments

Time (hrs)	**Absorbance (nm)**	**Concentration µg/ml**	**Amount of drug release**	**Cum % of drug release**

0	0	0	0	0
1	0.030	0.767	6.9	34.54±1.957
2	0.037	0.936	8.42	42.13±0.934
3	0.044	1.102	9.92	49.62±1.645
4	0.050	1.267	11.40	57.02±1.435
5	0.058	1.45	13.05	65.25±2.016
6	0.070	1.752	15.77	78.85±1.243
7	0.079	1.982	17.84	89.22±1.548
8	0.085	2.142	19.28	96.41±1.539

*Each value represents the mean±S.D. ofthree experiments

Time (hrs)	Absorbance (nm)	Concentration µg/ml	Amount of drugrelease	Cum % of drugrelease
0	0	0	0	0
1	0.014	0.352	3.17	15.87±1.524
2	0.016	0.406	3.65	18.27±1.432
3	0.024	0.62	5.58	27.90±1.586
4	0.028	0.724	6.52	32.62±1.351
5	0.034	0.863	7.77	38.85±2.054
6	0.038	0.959	8.63	43.17±2.364
7	0.045	1.142	10.27	51.39±1.561
8	0.053	1.342	12.08	60.42±1.429
9	0.060	1.516	13.65	68.25±1.357
10	0.066	1.661	14.95	74.76±1.438
11	0.071	1.790	16.11	80.56±1.215
12	0.075	1.882	16.94	84.73±1.365

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*Each value represents the mean±S.D. ofthree experiments

Tim e (hrs)	Absorbanc e(nm)	Concentratio nµg/ml	Amount ofdrug release	Cum % ofdrug release
0	0	0	0	0
1	0.016	0.42	3.84	19.2±1.251
2	0.020	0.52	4.68	23.42±2.015
3	0.024	0.62	5.62	28.13±2.036

4	0.03	0.77	6.93	34.65± 1.621
5	0.038	0.96	8.71	43.56±1.352
6	0.05	1.28	11.53	57.69±1.243
7	0.056	1.41	12.74	63.72±1.351
8	0.06	1.5	13.5	67.54±1.254
9	0.065	1.63	14.69	73.49±1.651
10	0.07	1.76	15.87	79.37±1.183
11	0.073	1.83	16.48	82.41±1.382
12	0.079	1.98	17.89	89.49±1.426

*Each value represents the mean±S.D. ofthree experiments

Time (hrs)	Absorbance (nm)	Concentration µg/ml	Amount of drugrelease	Cum % of drugrelease
0	0	0	0	0
1	0.0154	0.387	3.484	17.42±0.975
2	0.023	0.576	5.186	25.93±2.401
3	0.0316	0.790	7.118	35.59±1.246
4	0.042	1.05	9.492	47.46±1.652
5	0.05	1.257	11.316	56.58±1.752
6	0.053	1.33	12.044	60.22±1.462
7	0.060	1.503	13.528	67.64±1.325
8	0.066	1.67	15.054	75.27±1.425
9	0.073	1.826	16.438	82.19±1.546

10	0.077	1.940	17.466	87.33±1.159
11	0.081	2.031	18.286	91.43±1.879
12	0.083	2.085	18.77	93.85±1.042

*Each value represents the mean±S.D. ofthree experiments

Time (hrs)	Absorbance (nm)	Concentration µg/ml	Amount of drugrelease	Cum % of drugrelease
0	0	0	0	0
1	0.011	0.294	2.65	13.25±0.185
2	0.014	0.370	3.33	16.67±1.209
3	0.018	0.474	4.27	21.36±1.115
4	0.021	0.548	4.93	24.68±1.462
5	0.025	0.626	5.63	28.18±1.325
6	0.030	0.764	6.88	34.41±1.415
7	0.036	0.919	8.27	41.37±1.981
8	0.042	1.056	9.50	47.54±1.359
9	0.048	1.218	10.96	54.83±1.628
10	0.055	1.394	12.54	62.74±1.537
11	0.061	1.536	13.82	69.14±1.645
12	0.068	1.708	15.37	76.87±1.963

*Each value represents the mean±S.D. ofthree experiment

Time (hrs)	Absorbance (nm)	Concentration µg/ml	Amount of drugrelease	Cum % of drugrelease
0	0	0	0	0

1	0.013	0.349	3.14	15.73±1.652
2	0.019	0.498	4.49	22.45±1.518
3	0.025	0.649	5.84	29.21±1.175
4	0.032	0.817	7.35	36.78±1.264
5	0.036	0.916	8.24	41.23±2.063
6	0.041	1.046	9.42	47.11±2.143
7	0.046	1.167	10.50	52.54±1.648
8	0.052	1.303	11.73	58.67±1.364
9	0.057	1.447	13.02	65.12±1.751
10	0.064	1.618	14.56	72.82±1.462
11	0.069	1.744	15.69	78.48±1.273
12	0.072	1.822	16.40	82.02±1.682

*Each value represents the mean±S.D. ofthree experiments

Time (hrs)	Absorbance (nm)	Concentration µg/ml	Amount of drugrelease	Cum % of drugrelease
0	0	0	0	0
1	0.012	0.31	2.8	16±1.527
2	0.019	0.481	4.33	21.25±1.362
3	0.024	0.604	5.44	27.21±1.185
4	0.029	0.743	6.69	33.47±1.925
5	0.033	0.848	7.63	38.16±1.643
6	0.04	1.007	9.06	45.33±1.152
7	0.047	1.193	10.74	53.72±2.059

8	0.052	1.324	11.92	59.6±1.295
9	0.059	1.486	13.37	66.89±1.592
10	0.065	1.649	14.84	74.24±1.342
11	0.073	1.84	16.56	82.81±1.346
12	0.077	1.944	17.49	87.48±1.264

*Each value represents the mean±S.D. ofthree experiments

Time (hrs)	Absorbance (nm)	Concentration µg/ml	Amount of drugrelease	Cum % of drugrelease
0	0	0	0	0
1	0.009	0.232	2.094	10.47±2.145
2	0.012	0.308	2.78	13.92±0.978
3	0.017	0.435	3.92	19.63±1.689
4	0.021	0.537	4.84	24.20±2.146
5	0.024	0.624	5.62	28.14±1.507
6	0.031	0.795	7.16	35.81±1.307
7	0.037	0.936	8.43	42.16±1.624
8	0.042	1.073	9.66	48.33±1.364
9	0.048	1.209	10.88	54.42±1.759
10	0.052	1.323	11.91	59.56±1.158
11	0.056	1.408	12.67	63.39±2.076
12	0.058	1.472	13.25	66.25±1.379

*Each value represents the mean±S.D. ofthree experiments

Time (hrs)	Absorbance (nm)	Concentration µg/ml	Amount of drugrelease	Cum % of drugrelease
0	0	0	0	0
1	0.014	0.36	3.24	16.21±1.406
2	0.018	0.47	4.28	21.42±1.819
3	0.022	0.56	5.06	25.32±1.462
4	0.028	0.70	6.36	31.82±1.879
5	0.032	0.82	7.44	37.21±1.094
6	0.038	0.97	8.76	43.81±1.249
7	0.042	1.07	9.65	48.27±1.657
8	0.048	1.2	10.86	54.31±1.953
9	0.054	1.37	12.37	61.88±2.543
10	0.059	1.49	13.44	67.21±1.527
11	0.063	1.59	14.31	71.58±1.249
12	0.065	1.64	14.76	73.82±1.315

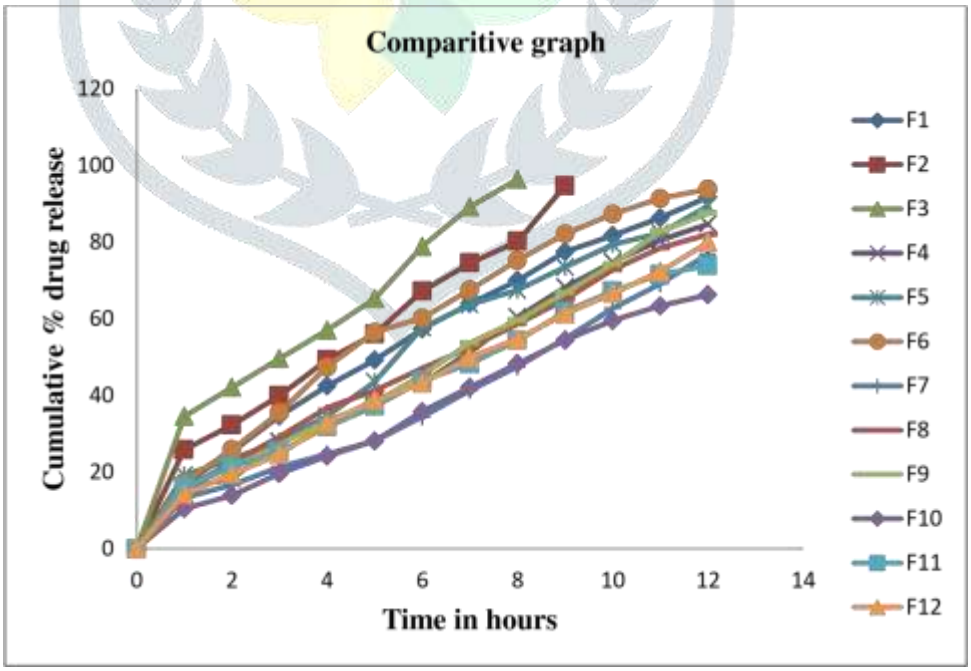
*Each value represents the mean±S.D. ofthree experiments

Time (hrs)	Absorbance (nm)	Concentration µg/ml	Amount of drugrelease	Cum % of drugrelease
0	0	0	0	0
1	0.0126	0.315	2.84	14.21±1.691
2	0.0173	0.433	3.9	19.50±1.052
3	0.021	0.547	4.92	24.63 ± 1.527

4	0.029	0.728	6.56	32.8±1.694
5	0.034	0.86	7.74	38.73±1.653
6	0.038	0.96	8.64	43.21±1.951
7	0.044	1.11	9.99	49.98±1.668
8	0.048	1.21	10.94	54.72±1.364
9	0.054	1.36	12.24	61.24±1.495
10	0.059	1.481	13.33	66.65±1.724
11	0.064	1.608	14.47	72.37±1.082
12	0.071	1.776	15.99	79.96±1.619

*Each value represents the mean±S.D. ofthree experiments

***IN -VITRO* CUMULATIVE PERCENTAGE OF DRUG RELEASE OF F1TO F12 FORMULATIONS**



CONCLUSION

The study showed that Glimepiride floating microspheres can be developed by Emulsion solvent diffusion-evaporation method and the results revealed that the formulation F9 shows desired release characterstics in the polymer ratio of (3:2) the hydroxy propyl methyl cellulose and ethyl cellulosein order to achieve the controlled release of drug up to 12 hours. Further *in- vivo* studies to be carried out to confirm

the formulation.

REFERENCES

1. Leon Lachman, Herbert A. Liberman. "The Theory and Practice OfIndustrial Pharmacy. 293-302.
2. Robinson Jr., Lee VHL. "Controlled drug delivery" fundamentals andapplications.2nd edition. Marceldekker; New York: 1978. p. 24-36.
3. Brahmankar DM, Jaiswal SB. "Biopharmaceutics and pharmacokinetics atreatise".1st edition. Vallabh prakashan; New Delhi: 1995. p.64-70.
4. Chein YW. Novel drug delivery systems. 2nd edition. Marcel dekker; New York: 1992. p.4-56
5. Ma N, Xu L, Wang Q, Zhang X, Zhang W, Li Y, Jin L, Li S. Development and evaluationof new sustained-release floating microspheres. Int J Pharm 2008; 358:82-90.
6. Karthikeyan D, Karthikeyan M, Ramasamy C. Development of floating microspheres toimprove oral bioavailability of cefpodoxime proxetil. Acta Pharmaceutical Sciencia 2010; 52: 101-104.
7. Diagnosis and Classification of Diabetes Mellitus, American Diabetes Association, Diabetes Care, 2004: 27.
8. Chandrashekar M, Sultanpur, Deepa K, Vijay Kumar S. Comprehensive Review onHba1cin Diagnosis of Diabetes Mellitus. Int J PharmRes 2010; 3: 119-122.
9. Ramachandran A, Das AK, Joshi SR, Yajnik CS *et al.*, Current Status of Diabetesin Indiaand Need for Novel Therapeutic Agents. J Assoc Physician India 2010; 58:7-9.
10. Narasimha Reddy D, Srinath MS, Hindustan Abdul Ahad, Kishore Kumar Reddy B *et al.*, Formulation and in-vitro Evaluation of Glimepiride and Parecoxib Combination Mucoadhesive Tablets. Scholars Research Library, 2011, 3:185-192.
11. Essentials ofpathophysiology. 2nd edition, carol Mattson porth, RN, MSN, PhD. Lippincott Williams & Wilkins, p.705-708.
12. Kumar, Cotrens, Robbins. "Basic pathology". 6th edition, p.560-574.
13. Carpenter MW, Coustan DR. Report of the Expert Committee on the Diagnosis andClassification ofDiabetes Mellitus. Diabetes Care 1997; 20:1183–97.
14. Gestational Diabetes Mellitus, DIABETES CARE, January2003:26.
15. Garber AJ, Handelsman Y, Einhorn D, Bergman DA, Bloomgarden ZT. Diagnosisand management of prediabetes in the continuum of hyperglycaemia: when do therisks of diabetes begin? A consensus statement from the American college of endocrinology and the American Association of clinical Endocrinologists. Endocrpract 2008; 14:933-46
16. Sumathy, Praveen Kumar, Ranjith Kumar K. Diagnosis of Diabetes Mellitus basedon RiskFactors. Int J Comput Appl2010; 10:1-4.
17. www.emedicinehealth.com.
18. www.mydiabetes.in/
19. en.wikipedia.org/wiki/Diabetes_mellitus_type_2.
20. V.N sharma. Essentials ofpharmacology, 3rd edition, p.383-84.