Chemometrics and its Applications in UV Spectrophotometry

Parixit Rohitbhai Prajapati[1,*], Deepika Natu Rathod[2], Vishalkumar Shashikant Modi[3], Tarashankar Basuri[4]

[1,3,4]Assistant Professor, [2]Research Scholar, Dept. of Quality Assurance Techniques
SSR College of Pharmacy, Silvassa, U.T. of Dadra & Nagar Haveli-396230

***Corresponding Author**
Email: parixitprajapati@gmail.com

Abstract

Chemometrics is the major developed branch which is widely employed in various pharmaceutical fields. Basically it is combination of chemical data along with mathematical and statistical treatment of the data using various mathematical models and software's. The developmental of various computational complexities along with the widespread growth of spectroscopy has used chemometrics for better results of the data obtained in spectroscopy. The review will highlight introduction to chemometrics, various chemometrics regression analysis techniques and applicability of chemometrics in UV visible spectrophotometry along with some application.

Keywords: Chemometrics, Classical Least Squares, Inverse Least Squares, Multi-linear regression, Principal Component Regression, Partial Least Squares Regression, UV Spectrophotometry.

Access this article online	
Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-2797.2016.00005.8

Introduction

Chemometrics can chiefly be described as the interaction of certainmathematical and statistical methods to chemical analysis and problems. Field of chemometrics started to grow around seventies and has widely influenced area of chemistry along with analytical chemistry. The science of chemometrics has developed because of changes in enormous data which is obtained in chemistry along with the evolution of new analytical techniques and technologies along with computer technology.

The development of computer technology has tremendously caused the wide growth of chemometrics since majority of multivariate methods utilized in chemometrics depend upon the ability and capability of computers to perform large calculations obtained by the chemometrics methods. In analytical chemistry chemometrics techniques has its applications in spectroscopy like UV-Visible spectrophotometry,NIR spectroscopy, fluorescence spectroscopy, chromate-graphy like Liquid Chromatography and also various other aspects of analytical chemistry like flow-injection analysis in pharmaceutical preparations.

The connection and usage of chemometrics and spectroscopy is as shown below[(1)]:

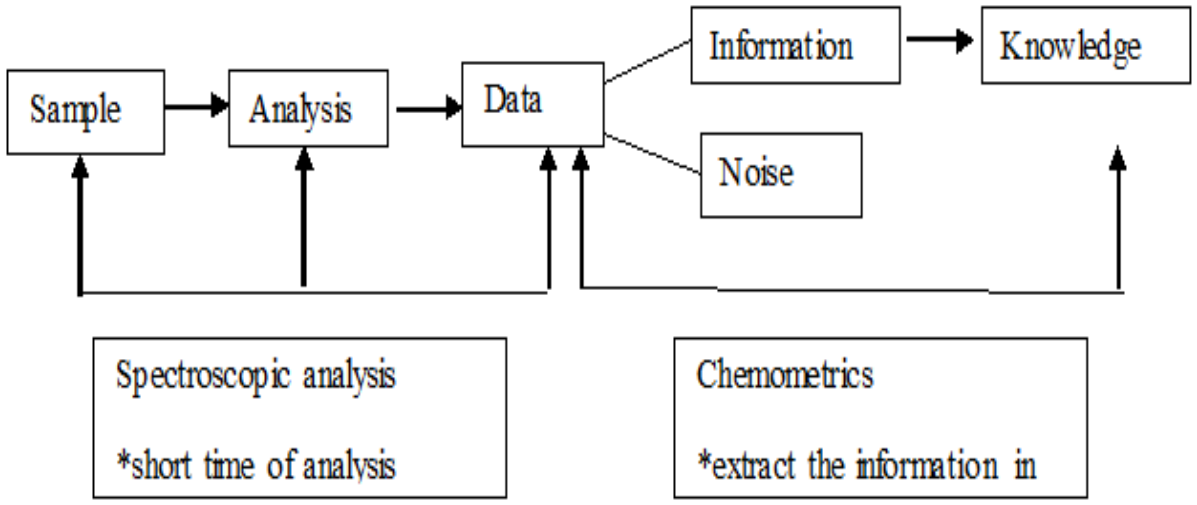

Fig. 1: Illustration of why spectroscopy and chemometrics work well in conjugation.

Basically the spectroscopic techniques are quick, which means analysis will take a few seconds or few minutes. Spectroscopy gives plenty of data for each sample, each combination, and each formulation which is analyzed. Any data obtained from the analysis can be divided into two parts: noise and information. The information will provide us with the knowledge of the sample and the noise will give us the non-informative part by which we can find a way to minimize or get rid of the noise in sample which effects the information obtained. In pharmaceutical industry various separation techniques for much analysis are carried out by Liquid chromatography with UV-Vis detection. Various parameters of qualitative and quantitative analysis like determination of content, identity and purity are performed using univariate methods like detection at single wavelength. Chemometrics uses multivariate methods hence it offers many advantages in qualitative as well as quantitative spectroscopic analysis.[1]

Different Aspects of Chemometrics: The name chemometrics can be divided into two terms namely chemo (from chemistry) and metric (meaning measurement). In short chemometrics is the term which deals with chemical data and how to obtain information from that data using mathematical models which must always be validated before they are applied. Experiments in chemometrics should be performed in such a way that all the experimental variables are varied which can be achieved by using experimental design.
Only multivariate data analysis approach should be implemented rather than univariate analysis in order to obtain more and deeper information.[2]

Principles of chemometrics are as follows:

1. Always use mathematical models for the connection, rationalization and interpretation of chemical data obtained by analysis.
2. Always include variability in the model, and handle the variability by means of distribution.
3. Always use statistical designs for planning sets of experiments when need to change conditions or optimizing etc. rather than changing only one factor and keeping others fixed.
4. Always use multivariate data analysis methods and show results as plots also perform the validation of mathematical model.[3]

Methods of Chemometrics

While implementing traditional concentration determination it is usually univariate by isolating one variable (e.g. wavelength maxima in UV). This traditional approach to data analysis is limited, imprecise and is wasted.

Example, a UV spectrum of any analyte is scanned; it will contain 500 data points. But while using, univariate approach for concentration determination (absorbance for any wavelength), then only 1% of the data will be used and 99.8% of data will be wasted.

Also in univariate determination measurement is sensitive to interfering factors. An analyst will not be able to differentiate between analyte specific signal and interfering signal. Hence in chemometrics multivariate measurement approach is implemented which involves multiple variables e.g. absorbance for a range of wavelengths. Hence multivariate methods has many advantages over univariate of which reducing noise and also removing of interfering signals is a major one, as looking at entire data set noise can be easily removed also interfering data profile differs significantly from the analyte. These advantages has been achieved due to computer power, efficiency and complexity whereas data is easily handled with common mathematical software packages, MATLAB is a common mathematical software employed.[4]

Multi-linear regression (MLR): One of the oldest methods and is now less used because of advancement in computational power. In UV this method will allow to establish a link between reduced number of wavelengths and any property of the analyte. Each wavelength of the data sets should be studied respectively and value obtained should be correlated with property to be studied. There are different modes of selecting the wavelength to be studied namely, forward, backward and stepwise. The correlation is fixed by the analyst and when the value of correlation is obtained it is then used for model calibration wavelengths. The model obtained is then computed between the found set of calibration wavelength and reference values of the property studied.[5]

Classical Least Squares (CLS): CLS involves application of MLR to conventional equation of beer-lambert law of spectroscopy:

$$A = KC \text{ (or } dA/d\lambda = KC)$$

Here matrix A is zero order absorbance matrix and $dA/d\lambda$ is derivative absorbance matrix, C is concentration matrix, and K is calibration coefficient matrix.

This method can only be used for systems when each constituent of sample is identified and known. If any contaminants are present in calibration mixture than this model will give false results about constituent concentrations.[6]

Inverse Least Squares (ILS): It is also known as p-matrix calibration, as it uses application of MLR to inverse equation of Beer-Lambert law of spectroscopy:

$$C = PA \text{ (or } C = P \times dA/d\lambda)$$

Here matrix A represent the zero-order absorbance, $dA/d\lambda$ represent derivative absorbance matrix, C is concentration matrix, and P is calibration coefficient matrix. One benefit over CLS method is that it can be

used for mixture of analyte whose composition is not known.

Advantages: ILS method can be employed for complex analyte which cannot be handled by CLS.

Disadvantages: Wavelength selection is difficult and time consuming, and the number of wavelengths will depend on number of calibration sample. Basically large number of samples is required for accurate calibration.[6]

Principal Component Regression (PCR): PCR is widely used model for data which has a large degree of covariance in independent variables or when ill conditioned matrix is present.

PCR implements PCA decomposition method before regression of the concentration information. Vectors with small magnitude are omitted in order to avoid co linearity problem. PCR will perform data decomposition by using only spectral information. PCR methods solve colliearity problem, band overlaps and other interactions by elimination of lower ranked principal components, which will reduce noise present within the system due to the availability of computer and mathematical software.[6]

Partial Least Squares Regression (PLS): PLS regression method is interrelated to both PCR and MLR in which PCR will find factors which will capture most of the variance within data before regression for the concentration variables while MLR will correlate both data and their concentrations.

This method will try to maximize the covariance hence correlate the variance and data together. Data decomposition is done by using spectral and concentration data.

PLS required fewer latent variables than PCR but this will not influence predictive ability of the method.In order to make a good estimation of additional parameters it becomes necessary to measure large number of samples under various changing conditions.[6]

Artificial Neural Networks (ANNs): Calibration becomes nonlinear when high levels of noise are present in such conditions ANN approach gives better results. ANNs were firstly designed to duplicate the function of the human brain. It consists of number of simple processing units linked by weighted modifiable interconnections.

When we compare ANN with MLR, it is a more flexible modeling methods as both linear and nonlinear functions can be combined in the processing units which allows more complex relationships between a high dimensional descriptor space and the given data, this in turn lead to better predictive power of the model.

Disadvantages

1. Major disadvantage of ANN is because of the complex model infrastructure.
2. In order to get robust calibrations the number of samples must be higher than number of weights to be estimated that means calibration samples used are large number.

Before forming ANNs, various methods like fast Fourier transform, PCA, and variance analysis are used for reducing the input dimensionality.[6]

UV-Vis Spectrophotometry and chemometrics: As UV-Visible spectrophotometry is a rapid, inexpensive analytical technique, hence it is highly suitable to control analysis and interpretation of pharmaceutical preparations containing components that absorb in the UV region. The only drawback is the presence of overlap between bands of different components will hinder it application due to the lack of specificity of UV-Visible absorption The development of various chemometrics techniques have enabled the application of UV-Visible spectrophotometry to the analysis of complex mixtures without the need for a prior separation.

Table 1: Few applications of UV Spectrophotometry implementing chemometrics

Sr. No.	Analyte	Chemometrics Methods	Ref. Number
1.	Levodopa and Beserazide	PLS, NPLS	7
2.	Cypermethrin and Tetramethrin	PLS	8
3.	Hydrocortisone, Nystatin and Oxytetracycline	PLS-1, PLS-2, PCR	9
4.	Dexamethasone, Polymixin B and Trimethoprim	PLS-1, PLS-2, PCR	10
5.	Moexipril and Hydrochlorthiazide	PLS, PCR	11
6.	Benazepril alone and in combination with Amlodipine	PLS, PCR	12
7.	Diphenylamine, Aniline and Phenol	PLS, PCR	13
8.	Amlodipine, Valsartan and Hydrochlorothiazide	PLS, PCR	14
9.	Nitrofurantoin, Furaltadone and Furazolidone	PLS	15
10.	2- Furfuraldehyde, 5-Hydroxymethylfurfuraldehyde and Malonaldehyde	PLS	16
11.	Pseudoephedrine hydrochloride and Ibuprofen	CLS, ILS, PCR, PLS	17
12.	Fexofenadine and Pseudoephedrine	PLS	18
13.	Caffeine, Dimenhydrinate and Acetoaminophen	PLS	19
14.	Triamterene and Leucovorin	PLS	20
15.	Mebendazole – Cambendazole and Mebendazole - Thiabendazole	PCR	21
16.	Phenytoin, Barbital and Caffeine	PLS, PCR	22
17.	Glafenine	CLS, MLR, PCR, PLS	23
18.	Acetylsalicylic acid and Ascorbic acid	PARAFAC, PLS	24
19.	Atenolol, sotalol, metoprolol, bisoprolol, propranolol, carvedilol, nebivolol	PLS	25
20	Imipramine, Amitriptyline and Perphenazine	PLS	26
21.	Hydrochlorothiazide and Amiloride	CLS, ILS, PCR, PLS	27
22.	Cilazapril and Hydrochlorothiazide	CLS, ILS, PCR, PLS	28
23.	Ciprofloxacin and Dexamethasone	PLS, MLR	29
24.		PCR, PLS	30
25.	Benazepril hydrochloride and Hydrochlorothiazide	CLS, PCR	31
26.	Paracetamol, Ibuprofen and Caffeine	PLS, PC-ANN	32
27.	Levodopa and Carbidopa	PLS	33
28.	Atrazine and Cyanazine	CLS, PCR, PLS	34
29.	Imipenem, Ciprofloxacin hydrochloride, Dexamethasone, Sodium phosphate, Paracetamol and Cilastatin sodium	PCR, PLS	35
30.	Guaiphenesine, Salbutamol sulfate, Acephylline, Piperazine, Bromohexine hydrochloride	PLS, PCR	36
31.	Metamizol, Acetaminophen and Caffeine	ILS, PCA	37

Conclusion

Chemometrics which has evolved as an emerging concept can be very precisely used to analyse various spectroscopic data and get useful results which can be used to get rid of wanted noise and use whole information. Hence analytical chemistry involving spectroscopic methods has been wisely benefited with the developed computational and mathematical power. The review is giving various methods of chemometrics which has been employed for the determination of various pharmaceutical formulations and get more precise results in very short time.

Conflicts of Interest: None

Source of Support: Nil

References

1. Wiberg K, PhD Thesis, Multivariate spectroscopic methods for the analysis of solutions Department of Analytical Chemistry, Arrhenius Laboratory, Stockholm University, 2004, Page No. 1-3.
2. Brereton RG, Chemometrics, Data Analysis for the Laboratory and Chemical Plant, University of Bristol, United Kingdom, 2003, Page No. 284- 307.
3. Wold S, Chemometrics, why, what and where to next? Journal of Pharmaceutical & Biomedical Analysis, Volume9, Issue. 8, 1991, Page No. 589-596.
4. Woody AD, Myles AJ, Brown SD, Transfer of multivariate spectral calibration models; a review, Chemometrics and

Intelligent Laboratory System, Volume 64, Issue 1, 2002, Page No. 181-192.
5. Roggo Y, Pascal C, Maurer L, Carmen L, Edmond A, Jent N,A review of near infrared spectroscopy and chemometrics in pharmaceutical technologies, Journal of Pharmaceutical and Biomedical Analysis, Volume 44, Issue 1, 2007, Page No. 683-700.
6. Gindy EH, Chemometrics in Pharmaceutical Analysis: An Introduction, Review, and Future Perspectives, Journal of AOAC International Volume 95, Issue 3, 2012, Page No. 609-619.
7. Coello J, Maspoch S, Simultaneous kinetic spectrophotometric determination of levodopa and beserazide by bi- and three- way partial least squares calibration, Talanta, Volume 53, Issue 3, 2000, Page No. 627-637.
8. Niazi A, Mohammad G, Orthogonal signal correction-partial least squares method for simultaneous spectrophotometric determination of cypermethrin and tetramethrin, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, Volume 69, Issue 4, 2008, Page No. 1165-1169.
9. Lemusgallego JM, Arroyo JP, spectrophotometric determination of hydrocortisone, nystatin and oxytetracycline in synthetic and pharmaceutical preparations based on various univariate and multivariate methods, AnalyticaChimicaActa, Volume 460, Issue 1, 2002, Page No. 85-97.
10. Lemusgallego JM, Arroyo JP, spectrophotometric resolution of ternary mixtures of dexamethasone, polymixin B and trimethoprim in synthetic and pharmaceutical formulation, AnalyticaChimicaActa ,Volume 437, Issue 2, 2001, Page No. 247-257.
11. Tawakkol S, Farouk M, Delaziz M, Hemdan A, Shehata M, Comparative study between univariate spectrophotometry and multivariate calibration as analytical tools for simultaneous quantitation of moexipril and hydrochlorthiazide, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, Volume 133, Issue 1, 2014, Page No. 300-306.
12. Farouk M, Delaziz M, Hemdan A, Shehata M, Tawakkol S, Comparative study between univariate spectrophotometry and multivariate calibration as analytical tools for simultaneous quantitation of benazepril alone and in combination with amlodipine, SpectrochimicaActa Part A: Molecular and Biomolecular Spectroscopy ,Volume 123, Issue 1, 2014, Page No. 473-481.
13. Bahramhem M, Morteza A, Fayazeh S, A Comparative study between PCR and PLS in simultaneous spectrophotometric determination of diphenylamine, aniline and phenol: effect of wavelength selection, Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, Volume 67, Issue 3-4, 2007, Page No. 958-965.
14. Hany WD, Said AH, Maissa YS, Badr AZ, Comparative study between derivative spectrophotometry and multivariate as analytical tools applied for the simultaneous quantitation of amlodipine, valsartan and hydrochlorothiazide, SpectrochimicaActa Part A: Molecular and Biomolecular Spectroscopy, Volume 113, Issue 1, 2013, Page No. 215-223.
15. Mahedero M, Galeanodiaz T, Galanpascual S, Resolution of ternary mixtures of nitrofurantoin, furaltadone and furazolidone by partial least- square analysis to the spectrophotometric signals after photo-decomposition, Journal of Pharmaceutical and Biomedical Analysis, Volume 29, Issue 3, 2002, Page No. 477-485.
16. Mantilla A, Pena A, Salinas F, Galena M, Simultaneous determination of 2- furfuraldehyde, 5- hydroxymethyl furfuraldehyde and malonaldehyde in mixtures by derivative spectrometry and partial least squares analysis, AnalyticaChimicaActa, Volume 276, Issue 1, 1993, Page No. 141-149.
17. Muratpalabiyik I, Dinc E, Zonur F, Simultaneous spectrophotometric determination of pseudoephedrine hydrochloride and ibuprofen in a pharmaceutical preparation using ratio spectra derivative spectrophotometry and multivariate calibration techniques, Journal of Pharmaceutical and Biomedical Analysis, Volume 34, Issue 3, 2004, Page No. 473-483.
18. Maggio RM, Castellano PM, Vignaduzzo SE, Kaufman TS, Alternative and improved method for the simultaneous determination of fexofenadine and pseudoephedrine in their combined tablet formulation, Journal of Pharmaceutical and Biomedical Analysis,Volume 45, Issue 5, 2007, Page No. 804-810.
19. Ayora MJ, Reguera MP, Diaz AM, Vallvey IF,Solid-phase UV spectroscopic multisensor for the simultaneous determination of caffeine, dimenhydrinate and acetoaminophen by using partial least squares multicalibration, Talanta, Volume 49, Issue 3, 1999, Page No. 691-701.
20. Meras ID, Mansilla AE, Lopez FS, Rodriguezgomez MJ, Determination of triamterene and leucovorin in biological fluids by UV derivative spectrophotometry and partial least-squares (pls-1) calibration, Journal of Pharmaceutical and Biomedical Analysis, Volume 27, Issue 1-2, 2002, Page No. 81-90.
21. Andrade SR, Scarminio IS, Nery MF, Oliveria AC, multivariate calibration methods to determine simultaneously mebendazole-cambendazole and mebendazole-thiabendazole in pharmaceutical preparations by UV - Visible spectrophotometry, Journal of Pharmaceutical and Biomedical Analysis, Volume 33, Issue 4, 2003, Page No. 655-665.
22. Abbaspour A, Mirazajani R, simultaneous determination of phenytoin, barbital and caffeine in pharmaceuticals by absorption (zero-order) UV spectra and first-order derivative spectra-multivariate calibration methods, Journal of Pharmaceutical and Biomedical Analysis, Volume 38, Issue 3, 2005, Page No. 420-427.
23. Ragehy M, Abbas S, Khateeb S, Stability indicating spectrophotometric methods for determination of glafenine using first derivative of ratio spectra and chemometric techniques, AnalyticaChimicaActa, Volume 461, Issue 1, 2002, Page No. 155-168.
24. Sena M, Fernandes J, Laercio R, Poppi R, Kubota L, Application of two and three way chemometric methods in the study of acetylsalicylic acid and ascorbic acid mixtures using ultraviolet spectrophotometry, Volume 409, Issue 1-2, 2000, Page No. 159-170.
25. Bourdon F, Lecoeur M, Odou P, Vaccher C, Foulon C, Complementarity of UV-PLS and HPLC for the simultaneous evaluation of antiemetic drugs, Talanta, Volume 120, Issue 1, 2014, Page No. 274-282.
26. Markopoulou CK, Malliou ET, Koundourellis JE, Application of two chemometric methods for the determination of imipramine, amitriptyline and perphenazine in content uniformity and drug dissolution studies, Journal of Pharmaceutical and Biomedical Analysis, Volume 37, Issue 2, 2005, Page No. 249-258.
27. Dinc E, Ustundag O, Chemometric resolution of a mixture containing hydrochlorothiazide and amiloride by absorption and derivative spectrophotometry, journal of pharmaceutical and biomedical analysis, Volume 29, Issue 1-2, 2002, Page No. 371-379.

28. Dinc E, Baleanu D, Spectroscopic quantitative determination of cilazapril and hydrochlorothiazide in tablets by chemometric methods, Journal of Pharmaceutical and Biomedical Analysis, Volume 30, Issue 3, 2002, Page No. 715-723.
29. Razuc M, Grunhut M, Elbio S, Garrido M, Fernandez B, Green method based on a flow- batch analyzer system for the simultaneous estimation of ciprofloxacin and dexamethasone in pharmaceuticals using chemometric applications, Talanta, Volume 115, Issue 1, 2013, Page No. 314-322.
30. Hameed E, Salam R, Hadad G, Chemometric assisted spectrophotometric methods and High Performance Liquid Chromatography (HPLC) for simultaneous determination of seven beta blockers in pharmaceutical products, SpectrochimicaActa Part A: Molecular and Biomolecular Spectroscopy, Volume 141, Issue 1, 2015, Page No. 278-286.
31. El-gindy A, Ashour A, Fattah L, Marwan S, Spectrophotometric determination of benazepril hydrochloride and hydrochlorothiazide in binary mixture using second derivative of ratio spectra and chemometric methods, Journal of Pharmaceutical and Biomedical analysis, Volume 25, Issue 2, 2001, Page No. 299-307.
32. Khoshayad M, Abdollahi H, Shariatpanahi M, Saadatfard A, Mohammad A, Simultaneous Spectrophotometric determination of paracetamol, ibuprofen and caffeine in pharmaceutical by chemometrics methods, SpectrochimicaActa Part A: Molecular and Biomolecular Spectroscopy, Volume 70, Issue 3, 2008, Page No. 491-499.
33. Damiani P, Moschetti A, Rovetto A, Bnavente F, Olivieri A, design and optimization of a chemometrics assisted spectrophotometric method for the simultaneous determination of levodopa and carbidopa in pharmaceutical products, , SpectrochimicaActa Part A: Molecular and Biomolecular Spectroscopy, Volume 543, Issue 1-2, 2005, Page No. 192-198.
34. Guowen Z, Junhui P, Simultaneous Spectrophotometric determination of atrazine and cyanazine by chemometric methods, SpectrochimicaActa Part A: Molecular And Biomolecular Spectroscopy ,Volume 78, Issue 1, 2011, Page No. 238-242.
35. Kosasy A, Aziz O, Magdy A, Elzahar N, Spectrophotometric and chemometric method for determination of imipenem, ciprofloxacin hydrochloride, dexamethasone, sodium phosphate, paracetamol and cilastatin sodium in human urine, SpectrochimicaActa Part A: Molecular And Biomolecular Spectroscopy, Volume 157, Issue 1, 2016, Page No. 26-33.
36. Gindy AL, Emra S, Heba S, Development and validation of chemometrics-assisted spectrophotometric and liquid chromatographic methods for the simultaneous determination of two multicomponent mixtures containing bronchiodilator drugs, journal of pharmaceutical and biomedical analysis, Volume 43, Issue 3, 2007, Page No. 973-982.
37. Erdal D, Baleanu D, Onur F, spectrophotometric multicomponent analysis of a mixture of metamizol, acetaminophen and caffeine in pharmaceutical formulations by two chemometric techniques, journal of pharmaceutical and biomedical analysis, Volume 26, Issue 5-6, 2001, Page No. 949-957.