Studia Universitatis "Vasile Goldiş", Seria Ştiinţele Vieţii
Vol. 22, issue 1, 2012, pp. 73-77

TOTAL QUALITY MANAGEMENT OF PHARMACEUTICAL PREPARATIONS CONTAINING VITAMIN E

Angela CAUNII[1*], Lucretia UDRESCU[1], Zoltan SZABADAI[1], George PRIBAC[2*], Monica BUTNARIU[3]
1Faculty of Pharmacy, University of Medicine and Pharmacy "Victor Babes", Timisoara, Romania, e–mail: angelacaunii@yahoo.com.
[2]Faculty of Medicine, Pharmacy and Dental Medicine, "Vasile Goldis" Western University, Arad, Romania
[3]Chemistry and Vegetal Biochemistry, Exact Sciences Department, Banat's University of Agricultural Sciences and Veterinary Medicine, Timisoara, Romania, e–mail: monicabutnariu@yahoo.com

ABSTRACT. Due to globalization and rapid processes in technology, production's competitiveness today is increasing. Producers must be permanently alert to find new ways to design, produce, sell and deliver their products. Today, quality is imperative.
Even low–cost pharmaceutical products are expected to have a good quality.
Degradation over time of many active substances with pharmaceutical interest, is a serious problem both regarding the industrial processes of obtaining, storage and use of these substances.
In pharmaceutical practice there are used drugs with advanced photosensitivity; problem of their degradation over time includes the action of light as a factor capable of contributing to their entire degradation. Ultraviolet radiation is not the subject of discussion, given that during the storage and use of therapeutics drugs, they are rarely exposed to this radiation.
Otherwise, the near ultraviolet radiation, with the spectral ranges 300–400nm, can be a real threat, especially in hospitals where the natural lighting is replaced by fluorescent tubes radiation.
This study aims identification of physic–chemical methods used in total quality management for medicinal products containing retinal acetate (Vitamin E), conditioned as gelatine capsules (pearls).
Key words: total quality management, gelatin capsules, Vitamin E

INTRODUCTION

An economic organization is maintaining only remaining competitive, this being achieved by orienting the organization towards quality by adopting and implementing a quality management system (Oprean *et al*, 2005).

Total quality management (TQM) focuses on continuous improvement processes, so they are visible, repeatable and measurable; it analyses and removes, in the same time, undesirable effects that may occur in production.

This strategy of quality assurance is not just a method for intern production processes, but extends to the managerial concerns beyond the product. The strategy also examines the way consumers use products in order to permanently improve its standing (Hulshof *et al*. 2003). Quality management is based on competing four stages: planning, execution, evaluation, improvement (Juran, 2000). Oxidation is usually considered being the most common form of lipid deterioration, including those used in the pharmaceutical industry, a process that leads to stagnation, leads to compounds with specific scent, polymerization and other reactions that cause the reduction of the period of validity and nutritional value of food (Meagher *et al*. 2001). Lipids abound in almost all food and many medicinal products, and most of them (>90%) are as triacylglycerol's, which esters of fatty acids and glycerol.

Two major components, involved in lipids oxidation are unsaturated fatty acids and oxygen (Yanishlieva *et al.* 1992). Oxidative degradation of lipids can be triggered by active oxygen and its related species, that are more active than triplet state oxygen molecules present in the air [Sim *et al*. 3004] and then exogenous agents (UV, ionizing radiation, heat) (Kris–Etherton *et al*. 2004). Within this context of total quality management, drugs photosensivity was the subject of many studies in which the experimental arrangement of controlled irradiation significantly differs from one laboratory and process to another. On the other hand, studies based on successive irradiation of a sample are affected by some error of principle:

- at repeated restart of irradiation source, it is difficult to replicate and control the period of transition, where the source reaches the stationary operating mode;
- at continuous irradiation of the sample, but samplings staple, the irradiated sample geometry changes during the investigation, so that additional sources of errors may also occur (Lampi *et al*. 1998).

As a result, purity control of pharmaceutical preparations is a necessity in the production phase, during storage and in different occasion such as the handling of litigation.

Purity control operation faces two problems that contribute to the sophistication of the problem.

First of all, bear in mind that the impurities are usually compounds with molecular structures similar to compound of interest: for this reason, control methods requires analytical specificity.

Secondly, impurities are minority component; therefore their detection is required in the present of the major component of interest. This means that the purity control methods must have an adequate sensitivity to capture impurities present even in traces. (Richardson *et al*. 2003). There are know many advanced analytical methods that meet these requirements, but most of the involve expensive laboratory equipment and highly qualified personnel.

In this study, the first part examines, extend in which the mobile phase liquid chromatography method (HPLC) meets the requirements set out above. The second part of the study discusses, as a second possibility, the record of middle infrared absorption spectrum (IR), which is a convenient and secure method to confirm the identity of pharmaceutical substances. This feature of IR spectrum due to wealth of information contained in the spectra.

Basically, it is totally unlikely that two different substances accidentally present identical IR spectra. (Westenhoefer *et al.* 2004)

MATERIALS AND METHODS

The objects of the study were retinal acetate gel capsules from the Romanian pharmaceutical industry.

In the first part of the study is presented HPLC analysis which was carried out with a □Nucleosil□ column with reverse stationary phase (C_{18}) of size 25x0.46 cm. The mobile phase pumping unit, mixer scheduled, degassing unit, ultraviolet absorption detector and visible absorption detector were produced by the company □Jasco□. The process of separation under isocratic run was controlled by specialized software □Borwin□ also obtained from the company □Jasco□. Methanol, used as a mobile phase, coming from the company □Merck□ was of HPLC grade.

Capsule content was dissolved in absolute ethanol (spectroscopic purity, □Uvasol□ quality, □Merck□ company).

The obtained solution was diluted in methanol (HPLC grade) to achieve a concentration compatible with the dynamic linearity of the detector. Of the final solution, 20 µl was injected into the chromatography column.

In the second part of the study, details of the retinal acetate recorded spectrum as a liquid film form in the spectral range 4000–1000 cm^{-1} are described. Recording spectrum as a liquid form was imposed by the retinal acetate liquid consistency. Liquid film, with the thickness of 0.05 mm, was conducted between two plates made of calcium fluoride crystal, a transparent material in the specified spectral range. Absorption spectrum was recorded with a spectrophotometer with Fourier transform (FTIR), ²640 Plus² model, a product of Jasco company.

RESULTS AND DISCUSSIONS

Figures 1 and 2 represent the chromatogram of vitamin E solution from the capsules. It is noted that the major component is accompanied by at least 7 components present in small quantities.

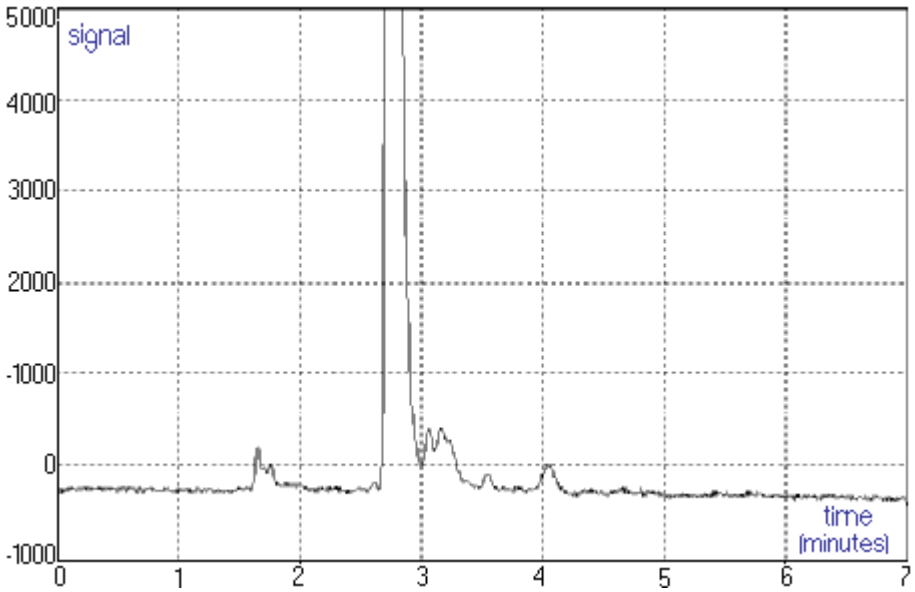

Fig. 1. Chromatogram of ethanolic solution of vitamin E capsules soft.

Studia Universitatis "Vasile Goldiş", Seria Ştiinţele Vieţii
Vol. 22, issue 1, 2012, pp. 73-77

Their presence stands out more clearly in Figure 2, where the signal detector scale was extended with a data processing program.

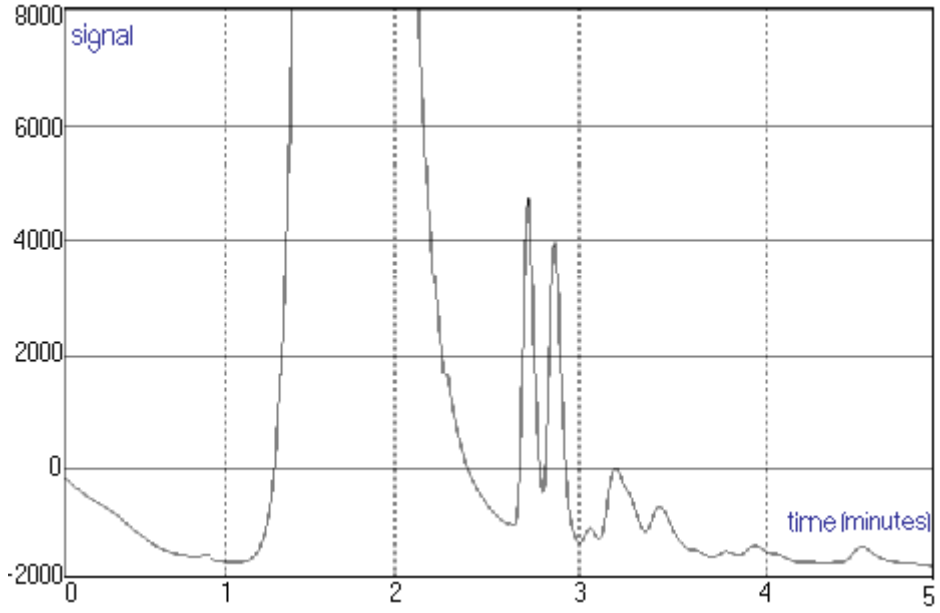

Fig. 2. Chromatogram of ethanolic solution of vitamin E capsules, soft

FT–IR stands for Fourier Transform InfraRed, the preferred method of infrared spectroscopy.

In infrared spectroscopy, IR radiation is passed through a sample. Some of the infrared radiation is absorbed by the sample and some of it is passed through (transmitted).

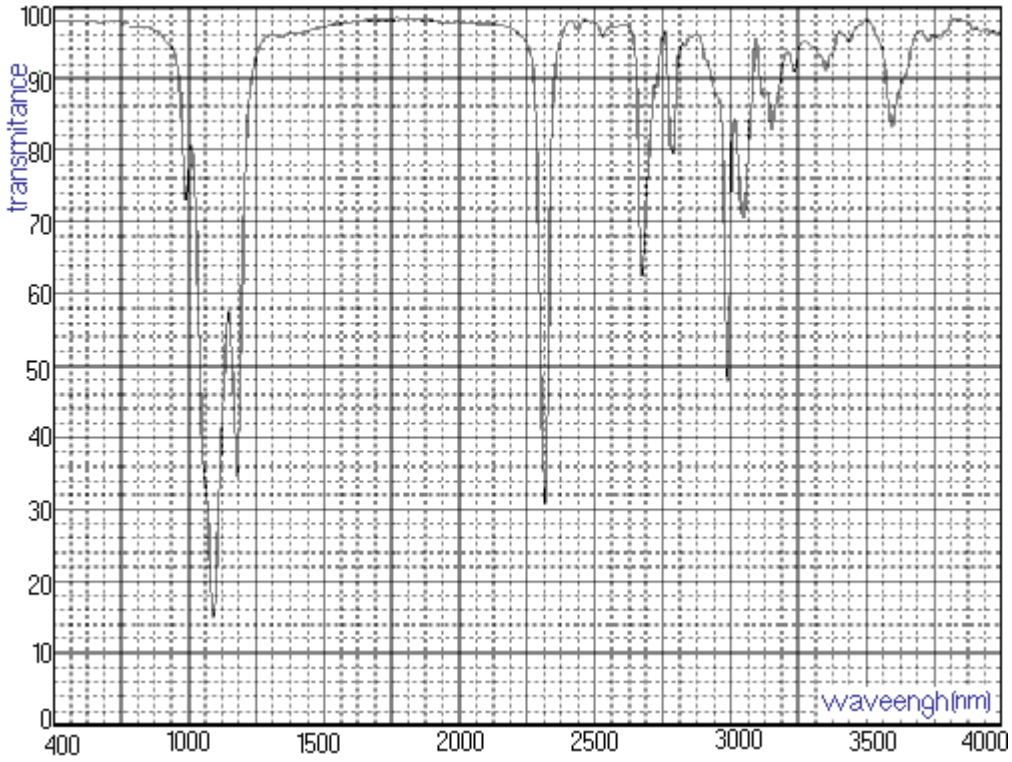

Fig. 3. IR absorption spectrum of retinal acetate.

One way to begin analyzing an infrared spectrum is to start at the high wavenumber end of the spectrum (typically 4000 cm–1) and look for the presence and absence of characteristic absorptions as you move toward lower wavenumbers.

The intensity of an absorption in the infrared spectrum is related to the change in dipole that occurs during the vibration.

The resulting spectrum represents the molecular absorption and transmission, creating a molecular fingerprint of the sample.

Like a fingerprint no two unique molecular structures produce the same infrared spectrum.

This makes infrared spectroscopy useful for several types of analysis.

The Infrared Spectroscopy is an extremely effective method for determining the presence or absence of a wide variety of functional groups in a molecule.

Figures 3 and 4 represent the recorded Infrared spectrum.

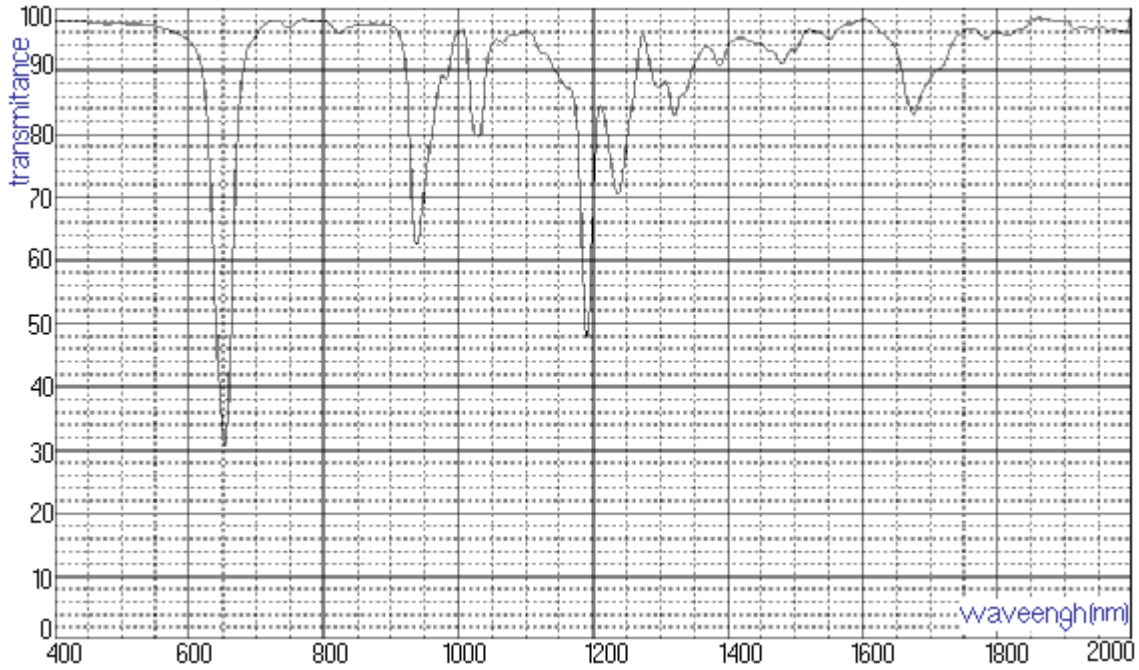

Fig. 4. IR absorption spectrum of retinol acetate

The normal way to approach interpretation of an infrared spectrum is to examine the functional group region to determine which groups might be present, then to note any unusually strong bands or particularly prominent patterns in the fingerprint region.

Matching the fingerprint region is a very rigorous test.

CONCLUSIONS

It is noted that HPLC method is able to capture small amounts of impurities even in the presence of a larger component of interest.

Also, that the interpretation of infrared spectra involves a rigorous mathematical formalism, but there can be made many empirical rules that allow correlation of the presence of an absorption band of the spectrum to a specific spectrum location with binds or molecular fragments.

In this respect, it speaks about vibration bands characteristic for chemical bonds or for functional groups.

The interpretation of infrared spectra involves the correlation of absorption bands in the spectrum of an unknown compound with the known absorption frequencies for types of bonds.

Bands position and their assignment to different chemical bonds or molecular fragments are shown in Table 2.

Weak bands locations (in cm^{-1}) are included in brackets.

Table 2. Interpretation of Infrared Spectra of retinol acetate

Signal position (cm^{-1})	Interpretation
3011	n (vinylidene group, C=C–H, *cis* configuration)
2927	n_{as} (H–C–H)
2856	n_{s} (H–C–H)
1747	n (C=O the ester group)
1464	n_{as} (H–C–H)
1378	n_{s} (H–C–H)
1210	n_{as} (C–O–C, characteristic cyclic ethers)
1168	n_{s} (C–O–C, characteristic cyclic ethers)
(1110)	n (C–O–C, characteristic cyclic ethers)
1084	n (H–C–H in cyclohexane nucleus)
(1018)	n (C–O–C, characteristic cyclic ethers, weak band in the IR, Raman intense)
(927)	n (vinylidene group, C=C–H) and n (–CH_2– in cyclohexane nucleus)
(866)	n (C–O–C, characteristic cyclic ethers, weak band in the IR, Raman intense)
730	$n_{rocking}$ (H–C–H)

The table will help users become more familiar with the process.

Significant for the identification of the source of an absorption band are intensity (weak, medium or strong), shape (broad or sharp), and position (cm^{-1}) in the spectrum. Therefore, we conclude that these methods correspond to the degree of precision required for use in the characteristic processes of total quality management.

REFERENCES

Sim, C.O. Hamdan, M.R. Ismail, Z. Ahmad, M.N. Assessment of Herbal Medicines by Chemometrics–Assisted Interpretation of FTIR Spectra, Journal Of Analytica Chimica Acta. 2004.

Cole C. (2001) Sunscreen protection in the ultraviolet A region: how to measure the effectiveness. Photodermatol. Photoimmunol. Photomed. 17: 2–10.

Hulshof Kf, Brussaard Jh, Kruizinga Ag, Telman J, Lowik Mr. Socio–economic status, dietary intake and 10 y trends: the Dutch National Food Consumption Survey. Eur. J. Clin. Nutr. 2003; 57: 128–37.

Juran, J.M., Planificarea calităţii, Editura Teora, 2000.

Kris–Etherton P.M., Hecker K.D., Binkoski A.E., Polyunsaturated fatty acids and cardiovascular health. Nutr Rev. 2004; 62: 414–426.

Lampi A–M. Kamal–Eldin A. Effect of a–and g–tocopherols on thermal polymerization of purified high–oleic sunflower triacylglycerols, J Amer Oil Chem Soc, 1998 75 1699–703.

Meagher EA., Barry OP., Lawson Ja., et al. Effects of vitamin E on lipid peroxidation in healthy persons. JAMA 2001; 285: 1178–1182e.

Oprean C., Kifor C. V., Suciu O. Managementul integrat al calitatii, Sibiu, Editura Universitatii "Lucian Blaga" din Sibiu, 2005.

Richardson DP., Affertsholt T., Asp NG., Bruce A., Grossklaus R., Howlett J., Pannemans D., Ross R.,Verhagen H.,Viechtbauer V. Passclai M.–Synthesis and review of existing processes. Eur J Nutr. 2003. 42(Suppl 1): 96–11.

Westenhoefer J., Bellisle F., Blundell JE., de Vries J., Edwards D., Kallus W., Milon H., Pannemans D., Tuijtelaars S., Tuorila H. Passclaim–Mental state and performance. Eur J Nutr. 2004, 43(Suppl 2): 85–117.

Yanishlieva N V and Marinova E M, Inhibited oxidation of lipids I Complex estimation of the antioxidative properties of natural and synthetic antioxidants, Fat Sci Techn, 1992 94 374–9.