LABIOFAM
Grupo Empresarial
DIRECCIÓN DE ENSAYOS CLÍNICOS

USE OF VIDATOX® 30CH IN PATIENTS WITH ADVANCED TUMORS

Author: Sirley González Laime. Licenciada en Ciencias Farmacéuticas.
Entity: Grupo Empresarial de Producciones Biofarmacéuticas y Químicas. LABIOFAM.
Country: Cuba.
Address: Ave 3raC No. 30007 e/300 y 302, Santa Fé, Municipio Playa, La Habana.
Telephone number: (537)2098561, cell (535)8240422
E-mail: sirley.gonzalez@labnet.com.cu, zclaime@infomed.sld.cu

[2013]

RESUMEN

Introducción: El cáncer constituye una de las primeras causas de muerte en el mundo. En nuestro país ocurre similar comportamiento, de ahí la importancia de incidir en modificar la calidad de vida de las personas que lo padecen. **Objetivo:** Describir el comportamiento de la capacidad funcional de pacientes con tumores malignos avanzados tratados con una formulación homeopática de la veneno del Escorpión *Rhopalurus junceus* (VIDATOX® 30CH) y la seguridad del producto. **Material y método:** Se realizó un estudio observacional, longitudinal prospectivo en los Servicios Médicos del Grupo Empresarial LABIOFAM. Se incluyeron 2261 pacientes con diagnóstico confirmado histológicamente. **Resultados:** En la muestra estudiada predominaron los sujetos de sexo masculino y los tumores de origen epitelial. Más del 70% de los pacientes tuvieron una evolución favorable, presentaron mejoría en su capacidad funcional y alivio del dolor. La mejor respuesta se obtuvo con la frecuencia de administración del VIDATOX® 30CH tres veces al día. No se reportaron eventos adversos severos. **Conclusiones:** El uso del producto en estudio resultó efectivo y seguro en la mejora de la capacidad funcional de los pacientes con tumores malignos en estadios avanzados.

Palabras clave: VIDATOX® 30CH, cáncer, homeopático, capacidad funcional, dolor, *Rhopalurus Junceus.*

ABSTRACT

Introduction: Cancer constitutes one of the first causes of death worldwide . Our country has the same situation ,that's why , the importance of modifying the life's quality in this kind of patients. **Objective:** To describe the behaviour of the functional capacity of patient with advanced tumors treated withan homeopathic formulation of the *Rhopalurus junceus* scorpion venom (VIDATOX® 30CH) and to describe the reliability of this product. **Materials and methods:** It was performed an observational and prospective study by the Medical Services of LABIOFAM. 2261 patients were included with confirmed histological diagnosis. **Results:** Prevailed masculine sex and epithelial tumors. More than 70% of the patients had a favorable evolution with the improvement of functional capacity and pain relief. The best answer was obtained with the frequency of administration of VIDATOX® 30CH three times a day. Severe adverse events were not reported. **Conclusions:** The use of VIDATOX® 30CH was effective and safe in the improvement of the functional capacity of the patients with advanced stage tumors.

Words key: VIDATOX® 30CH, cancer, homeopathic, functional capacity, pain, *Rhopalurus Junceus*.

INTRODUCTION

Introducing a drug to the market is preceded by a long period of basic,preclinic and clinic investigation, that concludes with the grant of the sanitary registration, once evaluated by the regulatory authority , the results of effectiveness and safety. But these data need to be enriched with the evidences that are obtained in the use of the medication under the conditions of the habitual medical practice [1,2.]

That´s why in the commercialization stage the pharmaco-surveillance plays an important role since it is in charge of the activities related with the detection, valuation, knowledge and prevention of the adverse reactions or any other problem related with the medicine [3-6.]

The regulatory organisms and the sanitary authorities of different countries are managed by norms, ordinances and legal documents, for the elaboration of the medicine post-commercialization studies with the purpose of knowing aspects related with their beneficial and harmful effects , as well as the characteristics related with their use according to the indications to which they were authoriz+-ed or under the habitual conditions of the clinical practice [7,8.]

Homeopathy is a therapeutic method that adapts perfectly to the tendency of the medical and human sciences called holistic medicine. Its use favors the reaction of a sick organism, stimulating the cure mechanisms. In theory, it is affirmed that the recovery of the lost balance during a disease is achieved by means of the stimulation of the immunologic system, by means of the Law of Similiarities [9-14.]

Cancer constitutes one of the first causes of death in the world, in Cuba the behaviour is similar. The health authorities pay special attention to this disease and they promote the search of alternatives that impact in the modification of the quality of people's life that suffer cancer.[15-23].

In Cuba, the venom of the Rhopalurus junceus scorpion , an endemic species, has been used with therapeutical objectives from the XIX century. In this sense, investigators of the Entrepreneurial Group LABIOFAM, have developed diverse researches with the venom of this scorpion[24].

VIDATOX® 30CH is an homeopathic product whose mother tincture is the venom of the Rhopalurus junceus scorpion in a centesimal dilution. Its ingestion by oral via is potentially non toxic. Its use doesn't exclude neither limit other conventional measures of treatment.

OBJECTIVES

General objective:

To describe the behaviour of the patients´s functional capacity with advanced malignant tumors treatied with VIDATOX® 30CH.

Specific objectives:

1. To characterize the patient carrier of advanced m++alignant tumors according to demographic and clinical variables.
2. To value(estimate) the functional capacity of the patient carrier of advanced malignant tumors treatied with VIDATOX® 30CH.
3. To identify the adverse events associated to the use of VIDATOX® 30CH.

MATERIAL AND METHOD

Context and classification of the investigation: It was carried out a prospective observational, longitudinal study of patients with diagnosis of advanced malignant tumors histologically confirmed that went to the Medical Services of the Entrepreneurial Group LABIOFAM during the period between March of the year 2011 until September of 2012.

Universe and sample: The universe was constituted by all the patients that went to the Medical Services of the Entrepreneurial Group, LABIOFAM during the period between March of the year 2011 until September of 2012. The sample was constituted by 2261 patients carrier of advanced malignant tumors histologically confirmed , with more than 18 years of age and that had in thier clinical history all the enough elements for their appropriate evaluation.

Variables: The main variables were age, sex, color of the skin, histopathological diagnosis , localization of the tumor, pain presence, daily frequency /-administration, period (date) in which they begin to experience improvement of the symptoms, evolution of the functional capacity and occurrence of some adverse event.

Procedures: The data coming from the variables of interest in the study, were gathered of the patients's clinical histories and they were transferred to a Model of Collection of Data made to that purpose. With this information a database of Microsoft Excel was made.
The evolution of the patient's functional capacity was classified according to the evaluation of the Indexes of Karnofsky and of ECOG, in the first consultation and in the last one .
The used scale was:

- Improved: Patients with improvements of symptoms and signs in the last consultation.
- Stable: Patients that doesn't manifest changes of symptoms and signs in the last consultation.
- Worsened: Patients that worsen symptoms and signs in the last consultation.

For the patient's final evaluation it was considered favorable one when analyzing the results presented by the patients, the pain was relieved and adverse events were not reported. On the contrary, it was considered unfavorable evolution when analyzing the results presented by the patients and the pain increased or severe adverse events were reported , they reached the category of worsened, .

Processing : The database was processed in an automatic way by means of the statistical processor SPSS version 11.5. The analysis of the demographic data and the clinical characteristics of the patients, was carried out by means of a descriptive analysis corresponding with the type of quantitative or qualitative variable. Summary measures were determined for qualitative variables (absolute number and percent) and quantitative variables

(arithmetic media(mean) and standard deviation) according to the data´s nature . The behaviour of the variables was described in the study and the association among them, by means of the application of the corresponding statistical procedures. For the statistical determinations it was taken into account an alpha equivalent to 0,05. The results were presented in tables and statistical graphics.

ANALYSIS OF THE RESULTS

A prevalence of the patients of the masculine sex was observed, represented by 1153 cases for 51%. The patients with ages between 71 and 80 years prevailed (615 cases for a 27,2%). The obtained data coincide with the ones described in the literature where it refers a prevalence of patients with malignant tumors in ages later to the reproductive age [25-28].

Table 1: Distribution of patients according to the age and sex.

GROUP OF AGE (years)	FEMENINE		MASCULINE		TOTAL	
	No.	%	No.	%	No.	%
Less than 31	61	2,7	59	2,6	120	5,3
31 to 40	59	2,6	161	7,1	219	9,7
41 to 50	276	12,2	120	5,3	396	17,5
51 to 60	276	12,2	298	13,2	574	25,4
61 to 70	140	6,2	136	6	276	12,2
71 to 80	276	12,2	339	15	615	27,2
More than de 80	20	0,9	41	1,8	61	2,7
Total	1108	49	1153	51	2261	100

Source :Clinical histories. Archives of the Medical Services of the Entrepreneurial Group LABIOFAM.

In ***Table 2*** it is observed a predominance of patients with lung malignant tumors (516 cases to a 22,8%), followed by patients with breast , colon and prostate cancer.

Table 2: Distribution of the patients according to the tumor´s location.

Location	Frecuency	Percentage
Lung	516	22,8
Breast	337	14,9
Colon	278	12,3
Prostate	278	12,3
Pancreas	138	6,1
Brain	99	4,4
Ovary	99	4,4
Úterus	59	2,6
Bone	41	1,8
Ureter	41	1,8
Rectus	41	1,8
Kidney	41	1,8
Other locations	300	13,5
Total	2261	100

Source :Clinical Histories. Archives of the Medical Services of the Entrepreneurial Group LABIOFAM.

To distribute the patients according to the histological diagnosis (***Tabla 3***), it was observed a predominance in patients carrier of tomors from epithelial origin. The carcinomes represented by 1268 cases (56,1%) and the adenocarcinomes are in the second place with 794 cases (35,1%).

Table 3: Distribution of the patients according to the histological diagnosis.

Histopathological diagnosis.		Frecuency	Percentage
Epithelial tumors	Carcinome	1268	56,1
	Adenocarcinome	794	35,1
	Glioblastome	99	4,4
Non epithelial tumors	Lymphoma	41	1,8
	Sarcoma	41	1,8
	Leukaemia	20	0,9
	Total	2261	100

Fuente: Historias Clínicas. Archivos de los Servicios Médicos del Grupo Empresarial LABIOFAM.

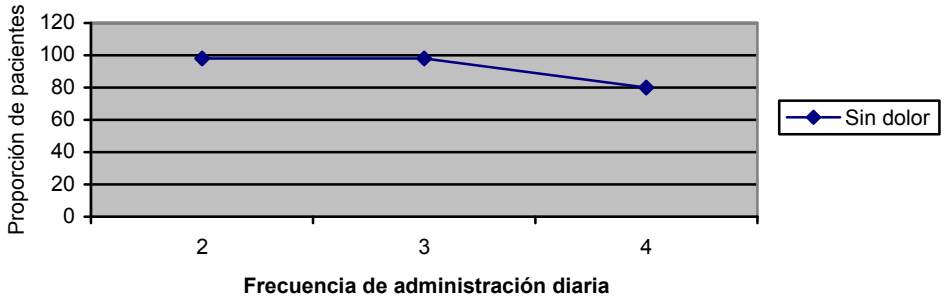
In the study, the indication of five drops of the product, with a daily frequency administration of two or three times a day prevailed in the 47,4% and 43,8% of the patients, respectively. In the table 4 and in the Graph 1, a greater proportion of patients without pain (symptom that most of the patients with this disease manifest) is observed in the group of patients that consumed VIDATOX® 30CH two or three times daily [29,30]. When determining the correlation rate in the Chi-Square of Pearson test to analyse the association between the presence of the pain and the daily frequency administration of VIDATOX® 30CH, an association statistically significant (p=0,012) was obtained. The corrected and classified residuals demonstrated that there were more cases, than the expected, of patients with pain that consumed VIDATOX® 30CH four times daily.

Table 4: Distribution of the patients according to the presence of pain and the daily frecuency administration of VIDATOX® 30CH

Daily administration frecuency.	Without pain		With pain		Total	
	No	%	No	%	No	%
Twice	1051	98,1	20	1,9	1072	100
Three times	971	98	20	2	990	100
Four times	159	80	40	20*	199	100
Total	2181	96,5	80	3,5	2261	100

Source:Clinical Histories . Archives of the Medical Services of the Entrepreneurial Group LABIOFAM. Chi-cuadrado of Pearson= 8,807 p=0,012. *Corrected and classified residuals greater than 1,96.

Gráfico 1: Porciento de pacientes sin dolor según frecuencia de administración diaria del VIDATOX 30CH



Source : Table 4

In the studied sample, the greatest percent showed favorable evolution of its functional capacity after the consumption of VIDATOX® 30CH [31-37]. Taken into account the product's daily frequency administration and the evolution from the functional capacity when concluding the study, it was observed that the patients that consumed the product in investigation, three times a day prevailed inside the group of patients that had experienced an improvement in the evolution of the functional capacity (825 cases for 66%). Table 5, Graph 2.

It can be appreciated that independently of the product daily frequency administration when carrying out the evolution of the functional capacity of the patients included in the study, most of these, reached the categories of stable and improved. The result of the statistical significance Chi- Square of Pearson test evidences that there is a statistically significant relation between the daily frequency administration of VIDATOX® 30CH and the evolution of the functional capacity with a reliability of 95% (p=0.038), being the daily frequency administration of three times the one with better evolution.
The result of the ranges's test with signs of Wilcoxon evidences that the changes in the patients's evolution in relation to this index, is statistically significant. Only two patients had an unfavorable evolution of the Karnofsky index when comparing it before and after the treatment [31].

In relation to the evolution according to the ECOG, most of the patients that evolved to an ECOG of two points consumed VIDATOX® 30CH two or three times daily. The result of the ranges's test with signs of Wilcoxon, evidences that the changes in the ECOG before and after the treatment are statistically significant. A prevalence of patients that evolved to an ECOG with punctuation between zero and two points was obtained.

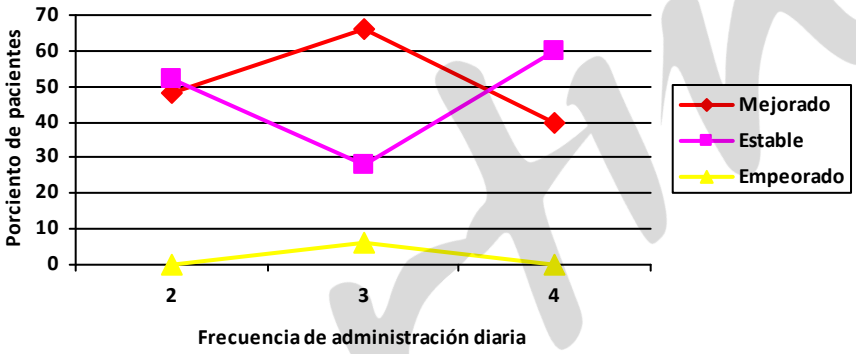
Table 5: Distribution of the patients according to the daily administration frecuency of VIDATOX® 30CH and the evolution of the functional capacity.

Evolution of the functional capacity	FRECUENCIA DE ADMINISTRACIÓN DIARIA DE VIDATOX® 30CH						TOTAL	
	Twice		Three times		Four times			
	No	%	No	%	No	%	No	%
Improved	601	48,1	825	66	500	40	1250	55,3
Stable	494	51,9	267	28	571	60	952	42,1
Worsened	0	0	4	6	0	0	59	2,6
Total	1072	100	990	100	199	100	2261	100

Source: Clinical Histories . Archives of the Medical Services of the Entrepreneurial Group LABIOFAM.

Chi-cuadrado of Pearson=10.141 p=0.038

Gráfico 2: Influencia de la frecuencia de administración diaria del VIDATOX® 30CH en la evolución de la capacidad funcional



Source: Table 5

The identification of the adverse events associated to the use of the VIDATOX® 30CH showed that only 18 (0,80%) patients reported adverse events after the consumption of the product in study. The 44 described adverse events, were classified as light according to the degree of intensity , regarding the approaches established by the WHO [38].

The irritation of the oral mucous was the most frequent adverse event, identified in 18 patients (40,1%), followed by the insomnia that 11 patients presented at the beginning of the treatment (25,0%). The nauseas and gingival bleeding were presented in 7 (16,7%) and 5 (11,4%) of them , respectively. Gastritis (2) and vomits (1) t were the adverse events less (fewer) referred.

The homeopathic products generally do not present adverse events although if aggravations are manifested to the beginning of their use in some patients for a short period of time , this aspect differs of what is presented with the use of allopathic medications.[39-

In the table 6 is analysed that the patients who had a favorable answer to the treatment consumed VIDATOX® 30CH three times a day. An association statistically significant was obtained when analysing a probability of the Chi- Square of Pearson test minor than 0,05 (p=0,049).

Table 6: Distribution of patients according to the daily administration frecuency of VIDATOX® 30CH and the answer to the treatment.

Daily frecuency administration.	Answer to the treatment.				Total	
	Favorable		Unfavorable			
	No	%	No	%	No.	%
Twice	754	70,4	317	29,6	1071	100
Three times	835	84,1*	158	15,9	993	100
Four times	100	50,8	97	49,2	197	100
Total	1689	74,7	572	25,3	2261	100

Source :Clinical Histories of the Medical Services of the Entrepreneurial Group LABIOFAM.
Chi-cuadrado of Pearson=6,029 p=0.049 * Corrected and classified residuals greater than 1.96.

CONCLUSIONS

1. The masculine patients of the third age with malignant tumors of epithelial origin in advanced stage , went more frecuently to the consultations of the Medical Services of the Entrepreneurial Group LABIOFAM.
2. Most of the patient carrier of malignant tumors in advanced stages , with pain and difficulty in their functional capacity, had a favorable evolution; especially those that used VIDATOX® 30CH three times daily .
3. VIDATOX® 30CH are a reliable product in human beings, since there were not acute adverse events during their consumption.

Bibliography :

1. View Point Part 2 Uppsala Monitoring Centre Uppsala: WHO Collaborating Centre for International Drug Monitoring. 2004; 3-66.
2. IV Conferencia Panamericana para la Armonización de la Reglamentación Farmacéutica. República Dominicana, 2005. Buenas Prácticas Clínicas. Documento para las Américas.
3. Trezz, JC. y Wesburd, G. Estudio de utilización de medicamentos: experiencia en un centro de salud en Villa Gobernador Gálvez, Santa Fe (Argentina). Archivo de Medicina Familiar. 2007. Vol.9 (4)159-163.
4. Brewer, T. and Colditz, GA. Postmarketing Surveillance and Adverse Drug Reactions. Current Perspectives and Future Needs. JAMA.1999; 281:824-829.
5. Laporte, JR.; Tognoni, G. Estudios de utilización de medicamentos y farmacovigilancia. En JR Laporte, G Tognoni (eds) Principios de epidemiología del medicamento, 2ª ed. Barcelona. Ediciones Científicas y Técnicas, 1993; 1-24.
6. Álvarez, F. Farmacoepidemiología. Estudios de Utilización de Medicamentos. Parte I: Concepto y metodología. Seguim Farmacoter 2004; 2(3):129-136.

7. González, B.; López, A.; Cabeza, A.; Díaz, JA.; Ortún, V. y Álamo, F. Estudios de Utilización de Medicamentos y registros de datos en Atención Primaria. 2005; 2-11.
8. Sackett, DL.; Scott, W.; Rosenberg, W. y Brian, R. Medicina basada en la evidencia, cómo ejercer y enseñar MBE. Churchill communications Europe España ed. Madrid.1997.
9. Ernst, E. Homeopathy: past, present and future. Br J Clin Pharmacol. 1997; 44:435-7.
10. Cook, T. Homeopathic medicine today, Chapter 3 Homeopathic pharmacy. 2004.
11. Laza, D.; Rodríguez, I. y Sardiña, G. La homeopatía en el tratamiento del cáncer. Análisis de información. Revista Cubana de Plantas Medicinales; 2002, 7(1), p: 6-13. Disponible en URL: www.bvs.sld.cu/revistas/pla/vol7_01_02/pla02102.pdf.
12. Edzard Ernst. A systematic review of homeopathy. Brithis Journal of Clinical Pharmacology. 2002; 54(6): 577-582.
13. Gold, P.W; Novella, S.; Roy, R.; Marcus, D.; Bell, I.; Davidovitch, N. *et al* Homeopathy quackery or a key to the future of medice? Homeopathy. 2008; 97(1), 28-33.
14. Phillips Jr. Magical thinkin in complementary and alternative medicine, Skeptical Inquirer Magazine. 2001; Nov-Dic.
15. Ben-Arye, E.; Saleem, M.; Nejmi, M.; Schiff, E.; Mutafoglu, K.; Afifi, F. *et al*. Integrative oncology research in the Middle East: weaving traditional and complementary medicine in supportive care. Support Care Cancer. 2012; (20):557–564.
16. Frenkel, M. Homeopathy in cancer care. Altern Ther Health Med. 2005; 16:12-16.
17. Walach H, Jonas WB. and Ives J. Research on homeopathy: state of the art. J Altern Complement Med. 2005; 11:813-829.
18. Colectivo de autores. El manual Merk, Tomo V, undécima edición. 2007; 1215-31.
19. Organización Panamericana de la Salud. Plan de acción regional de prevención y control del Cáncer. Washington DC; 2008. Disponible en: http://www.paho.org/Spanish/AD/DPC/NC/pcc-stakeholders-08.htm.
20. Cancer. Descriptive note febrero 2011; N^0 297. Disponible en: http://www.who.int/mediacentre/factsheets/fs297/es/index.html.
21. Colectivo de autores. Anuario Estadístico de Salud. Dirección Nacional de Registros Médicos y Estadísticas de Salud. MINSAP. 2011Jeschke, E.; Ostermann, T.; Tabali, M.; Vollmar, HC.; Kröz, M.; Bockelbrink, A. *et al.* BMC Pharmacotherapy of elderly patients in everyday anthroposophic medical practice: a prospective, multicenter observational study Geriatrics. 2010; (10):48.
22. Redondo, B.F.; Chacón, M.; Grau, J.A. y Nicot, L. Evaluación de la sintomatología más frecuente en el paciente oncológico en fase terminal. Rev Cubana Oncol. 1998; 4(2):83-6.
23. Abalo, JR. La calidad de vida en el enfermo con cáncer avanzado. En: Gómez Sancho M, ed. Cuidados paliativos e intervención psicosocial en enfermos terminales. Las Palmas de Gran Canaria: ICEPSS, 2 ed.1998; 140-64.
24. Riverón, MN.; López, RJ.; Viera, E.; Tena SI; Alvarez, MC. Sintomatología de la picadura del alacrán azul cubano Rhopalurus junceus. 2012; 5(1):13-18.
25. Molassiotisa, A.; Pantelib, V.; Patirakib, E.; Ozdenc, G.; Platind, N.; Madsene, E.; *et al.* Complementary and alternative medicine use in lung cancer patients in eight European countries. Complementary Therapies in Clinical Practice. 2006; 12:34–39.
26. Integrating a geriatric evaluation in the clinical setting. Martine Extermann, Semin Radiat Oncology. 2012; (22):272-276.
27. Kasmierska, J. Assessment of health status in elderly patients with cancer. Reports of practical oncology and radiotherapy. 2012.

28. Gosney, MA. Clínical assessment of elderly people with cáncer. Review. Lancet oncology. 2005; (6):790-797.
29. Yorke J., Brettle A. and Molassiotis A. Nonpharmacological interventions for managing respiratory symptoms in lung cancer. Downloaded from crd.sagepub.com at Instituto Europeo di Oncologia on October 25, 2012. Chronic Respiratory Disease 2012; 9(2):117–129.
30. Katz, N.P. The measurement of symptoms and side effects in clinical trials of chronic pain. Contemporary Clinical Trials. 2012; (33):903-911.
31. Karnofsky, D.A.; Abelmann, W.H. and Graver, L.F. The use of nitrogen mustards in the palliative treatment of carcinom. CANCER. 1948; 1:634-56.
32. Rostock, M.; Naumann, J.; Guethlin, C.; Guenther, L.; Bartsch, H. and, Walach, H. "Classical homeopathy in the treatment of cancer patients - a prospective observational study of two independent cohorts" 3BMC Cancer. 2011; 11:19 http://www.biomedcentral.com/1471-2407/11/19.
33. Sanz VJ. La homeopatía ¡vaya timo! Editorial Laetoli. 2010. ISBN; 978-84-92422-18-0.
34. Shang, A.; Huwiler-Muntener, K.; Nartey, L.; Juni, P.; Dorig, S.; Sterne, AJ. *et al.* Are the clinical effects of homeopathy placebo effects? Comparative study of placebo-controlled trials of homeopathy and allopathy. Lancet. 2005; 366(9487):pp. 726-732.
35. Zapka J., Taplin SH., Ganz P., Grunfeld E., Sterba K. Multilevel Factors Affecting Quality: Examples From the Cancer Care Continuum Journal of the National Cancer Institute Monographs. 2012: 44:11–19.
36. Ioannidis, JP. and Lau, J. Completeness of safety reporting in randomized trials. An evaluation of 7 medical areas. JAMA. 2001; 285:437-443.
37. Rostock, M.; Naumann, J.; Guethlin, C.; Guenther, L.; Bartsch, H. and, Walach, H. "Classical homeopathy in the treatment of cancer patients - a prospective observational study of two independent cohorts" 3BMC Cancer. 2011; 11:19 http://www.biomedcentral.com/1471-2407/11/19.
38. Naranjo, CA. y Busto, UE. Reacciones adversas a medicamentos. En: Métodos de farmacología clínica, capítulo 14, OMS-OPS, 1992.
39. Dantas, F. and Rampes, H. Do homeopathic medicines provoke adverse effects? British Homeopathic Journal. 2000; 89:S35-38.
40. Macias, EC. y Asbun, J. Frecuencia de eventos adversos en prescripciones homeopáticas en el Hospital Juárez de México. Rev. Hosp. Jua Mex. 2008; 75(3):190-97.
41. Endrizzi, C.; Rossi, E.; Crudell, L.; Garibaldi, D. Harm in homeopathy: aggravations, adverse drug events or medication errors? Homeopathy. 2005; 94(4):233-40.
42. Gravia, S. and Ernst, E. Homeopathic aggravations: a systematic review of randomized, placebo-controlled clinical trials. Homeopathy. 2003; 92:92-8.