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Effect of Antiulcer on the Liver functions

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Abstract:

This study was done in Samarra city from 2-8-2015 until 22-12-2015 and 105 sample was collectedand divided to three groups. The first group 35 patientswere take Ranitidine as antiulcer drug and 35 patients were take Omeprazole antiulcer drug and 35 subjects as control. Patientscomparison were done between each group with control get a result if there is any effect on Liver function that the result were decrease in Alanine transferese (ALT), Aspartate transferese (AST), Alkaline phosphatase (ALP) and serum Total Protein (S. Total Protein), and we observed both of Ranitidine and Omeprazole not effect on total serum bilirubin (T.S.B) . The comparison between the two drugs in the impact on function convergent.

Key words: Ranitidine ,Omeprazole, antiulcer drug, Liver function

الخلاصة:

تمت الدراسة في مدينة سامراء واستمرت للمدة 2-8-2015 الى 22-12-2015 حيث تم جمع 105 عينة وكانت مقسمة بواقع 35 عينة لأشخاص مصابين بقرحة المعدة ويتناولون رانتدين و35 عينة لأشخاص أيضا مصابين بقرحة المعدة ولكنهم يتعاطون الأوميبرازول ، وتمت مقارنة كل فئة منهما على حدا مع أشخاص أصحاء (مجموعة ضابطة) ، ثم قارنا عينات المرضى فيما بينهم لنستدل على حالة وظائف الكبد في كل مقارنة فوجدنا نتائج تشير الى أن مضادات التقرح ساهمت في خفض مستويات (ALT,AST, ALP, S.Total Protein). ووجدنا تأثير هذين العقارين في رفع مستوى (TSB) قليلاً، وكانت المقارنة بين الدوائين في التأثير على الوظائف متقاربه.

Introduction:

There are several organs involved in the digestion of food. This starts at the mouth, pharynx, esophagus, stomach, small intestine, large Intestine and ends at the anus[1].

A major digestive organ is the stomach. Within its mucosa are millions of embedded gastric glands. Their secretions are vital to the functioning of the organ. There are many specialized cells of the Gastrointestinal tract. These include the various cells of the gastric glands, taste cells, pancreatic duct cells, enterocytes and microfold cells.

Stomach secrete Gastric acid (informally gastric juice), produced in thestomach plays a vital role in the digestion process, it mainly contains hydrochloric acid and sodium chloride. A peptide hormone gastrin produced by Gastro cells in the gastric glands, stimulates the production of gastric juice which activates the digestive enzymes. Pepsinogen is a precursor enzyme (zymogen) produced by the gastric chief cells and gastric acid activates this to the enzyme pepsin which begins the digestion of proteins[2].

Peptic ulcer disease

Peptic ulcer or stomach ulcer, is a break in the lining of the stomach , first part of the small intestine, or occasionally the lower esophagus[4], An ulcer in the stomach is known as a gastric ulcer while that in the first part of the intestines is known as a duodenal ulcer. The most common symptoms are waking at night with upper abdominal pain or upper abdominal pain that improves with eating. The pain is often described as a burning or dull ache.

Other symptoms include belching, vomiting, weight loss, or poor appetite . About a third of older people have no symptoms[6]. Complications may include bleeding ,perforation , and block of the stomach . Bleeding occurs in as many as 15% of people[5].

Treatment of Ulcer

Ranitidine, sold under the trade name **Zantac(R),** is a medication that decreases stomach acid production.[5] It is commonly used in treatment of peptic ulcer, gastroesophageal reflux disease, and Zollinger–Ellison syndrome.[13] It can be taken by mouth, by injectionintramuscular, or intravenous.[5]

Mechanism of action:

Ranitidine is H2 receptor antagonist, a competitive, reversible inhibitor of the action of histamine at the histamine H2 receptors found in gastric parietal cells. This results in decreased gastric acid secretion and gastric volume, and reduced hydrogen ion concentration[7].

Omeprazole, sold under the brand names **Prilosec(R)** and **Losec(R)** among others, is a medication used to treat gastroesophageal reflux, peptic ulcer, and Zollinger–Ellison syndrome, It is also used to prevent upper gastrointestinal bleeding in people who are at high risk, It is taken by mouth.[8]

Mechanism of action: Omeprazole is a selective proton pump inhibitor. It suppresses stomach acid secretion by specific inhibition of the H+/K+-ATPase system found at the secretory surface of gastric parietal cells. Because this enzyme system is regarded as the acid (proton, or H+) pump within the gastric mucosa, omeprazole inhibits the final step of acid production. Omeprazole also inhibits both basal and stimulated acid secretion irrespective of the stimulus.[9]

The liver performs many different functions yet is also a discrete organ, and many of its functions interrelate with one another. This becomes especially evident in abnormalities of the liver, because many of its functions are disturbed simultaneously. The role of liver in the metabolism can summarized as the following; The liver is a large, chemically reactant pool of cells that have a high rate of metabolism, sharing substrates and energy from one metabolic system to another, processing and synthesizing multiple substances that are transported to other areas of the body, and performing myriad other metabolic functions. For these reasons, a major share of the entire discipline of biochemistry isdevoted to the metabolic reactions in the liver.[10]

The aminotransferases constitute a group of enzymes that catalyze the interconversion of amino acid and alpha-ketoacids by transfer of amino groups. This group consist of two enzymes.(11,12,13)

The enzymes AST Aspartate aminotransferaseand ALT Alanine aminotransferase are widely distributed throughout the body. Aspartate transaminase is found primarily in the heart, liver, skeletal muscle, and kidney, whereas ALT is found primarily in the liver and kidney with a lesser amounts in heart and skeletal muscle.[14]

ALP Alkaline phosphatase is a group of relatively non-specific enzymes which catalyze the alkaline hydrolysis of a large variety of naturally occurring and synthetic substrates, but the natural substrates on which they act in the body are not known.[15]

In healthy adults,this is mainly derived from the liver, bones and in lesser amounts from intestines, placenta, kidneys and leukocytes[16].

Serum Total Protein also known as total protein, is a biochemical test for measuring the total amount of protein in serum.[17]

Protein in the plasma is made up of albumin and globulin. The globulin in turn is made up of α1, α2, β, and γ globulins.[17]

Proteins, the structural and functional components of a cell. The functional components serve as biocatalysts

(enzymes), regulator of metabolism, (hormones) [18]. Plasma proteins and tissue proteins share the same amino acid pool (building blocks of proteins)

Bilirubin is created by the activity of biliverdin reductase on biliverdin a green tetrapyrrolic bile pigment that is also a product of heme catabolism. Bilirubin, when oxidized, reverts to become biliverdin once again. This cycle, in addition to the demonstration of the potent antioxidant activity of bilirubin(19,20,21,22) has led to the hypothesis that bilirubin's main physiologic role is as a cellular antioxidant.

The active chemical medium of the liver is well known for its ability to detoxify or excrete into the bile many drugs, including; Antiulcer drug as Omeprazole and Ranitidine.

Materials and methods

Collection of samples:

105 blood sample were collected, and let them until clotting, samples include three groups:

Group I: - patients have gastroulcer use Ranitidine (35 Samples)

Group II: - patients have gastroulcer use Omeprazole (35 Samples)

Group III: control without gastroulcer and not use any antiulcer drugs (35 Samples)

5ml of blood sample is taken by disposable syringe and put the sample in Gel Tube. serum separated after clotting by centrifuge in room temperature.

Determination of Serum Alanine Aminotransferaseactivity:

the level of Alanine Aminotransferasein the serum estimated by using Enzymatic method using kit for assessing the Aspartate Transaminase processed by the company BT (Made in Turkey).[23]

Determination of serum Aspartate Transaminase activity:

the level of Aspartate Transaminase in the serum by using Enzymatic method using kit for assessing the Aspartate Transaminase processed by the company BT (Made in Turkey).[24]

Determination of serum Alkaline Phosphatase activity:

Serum Alkaline Phosphatase activity was measured using several analysis (kit) manufactured by the company (BioMerieux)[25]

Determination of Serum Total Protein activity:

Serum Total Protein concentration was measured using analysis (kit) manufactured by the company BIOLABO[26]

Total Serum Bilirubin parameter

capillary tube used to collect Serum and measure TSB by TSB Meter.

statistical analysis

The samples for study data collection and analysis using statistical system (Statistical Package of Social Sciences) (SPSS Chicago ,Lillian's and U.S.A)) WindowIt has been compared to the use of the analysis of averages Analysis compart means ((paired Samples T test))$P<0.05$ set as statistically significant.

Result & Discussion:

Aspartate aminotransferase AST)&Alanine aminotransferase (ALT) Alkaline Phosphatase (ALP)

The results showed that there are significant differences in the level of ALT,

AST & ALP $P\leq0.05$, Among people who take anti-ulcer drugs, Compared with healthy people, The study showed a decrease in the level of liver enzymes compared with healthy people. This study did not agree with the findings of each of (Ramrakhiani s, et al. 1998) [27] On medication (Ranitidine) and reached (Jochem v, et al, 1992) [28] On medication (Omeprazole), and not to be such a consensus because both researchers have conducted research for 14 days. The study showed a decrease in the level of enzymes, Because long-term use of the drug, which

leads to a change in liver function. This agrees with the (Middle East medical Index).[29][30]

The study also found no significant differences in the level of enzymes between the users of these two drugs, as these drugs have the same effect on the enzymes[29][30].

Table 1: show effect of ranitidine and omeprazole compared with control on level of serum alanine aminotransferase in the body.

Parameter		Number	mean±SD
Alanine aminotransferase (ALT)	Control	35	28.7691±8.04320
	Ranitidine	35	12.3800±16.04936
	Omeprazole	35	7.5753±8.62951

There is a significant difference (P≤0.05)

Alanine aminotransferase (ALT) Level

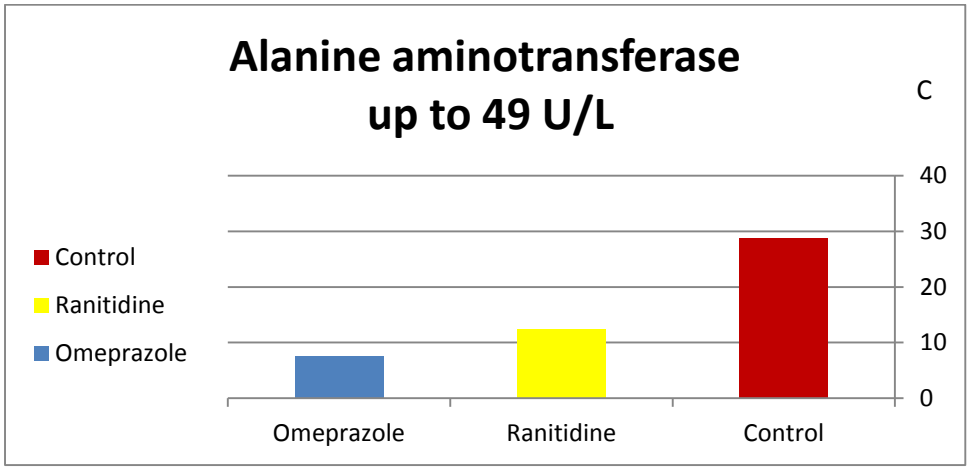

Chart 1: Effect of ranitidine and omeprazole compared with control on level of serumalanine aminotransferase in the body.

Table2: Effect of ranitidine and omeprazole compared control on level of serum aspartate aminotransferase in the body.

Parameter		Number	mean±SD
Aspartate aminotransferase (AST)	Control	35	29.6922±7.92997
	Ranitidine	35	9.1400±9.70541
	Omeprazole	35	7.5670±8.62437

There is a significant difference (P≤0.05)

Aspartate aminotransferase (AST) Level

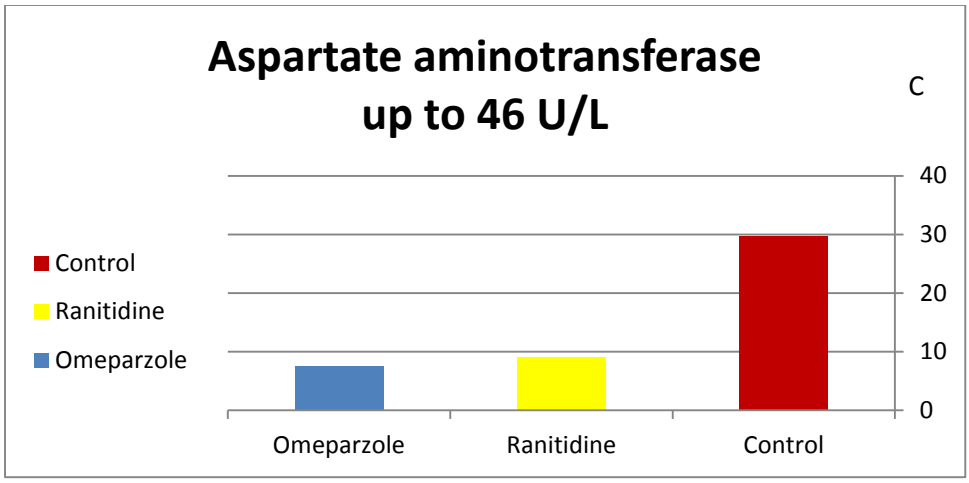

Chart 2: Effect of ranitidine and omeprazole compared with control on level of serum aspartate aminotransferase in the body.

Table 3: Effect of ranitidine and omeprazole and control on level of serum alkaline phosphatase in the body.

Parameter		Number	mean±SD
Alkaline Phosphatase(ALP)	Control	35	10.7354±1.38285
	Ranitidine	35	7.5311±2.48107
	Omeprazole	35	8.0416±3.04007

There is a significant difference (P≤0.05)

Alkaline Phosphatase (ALP) Level

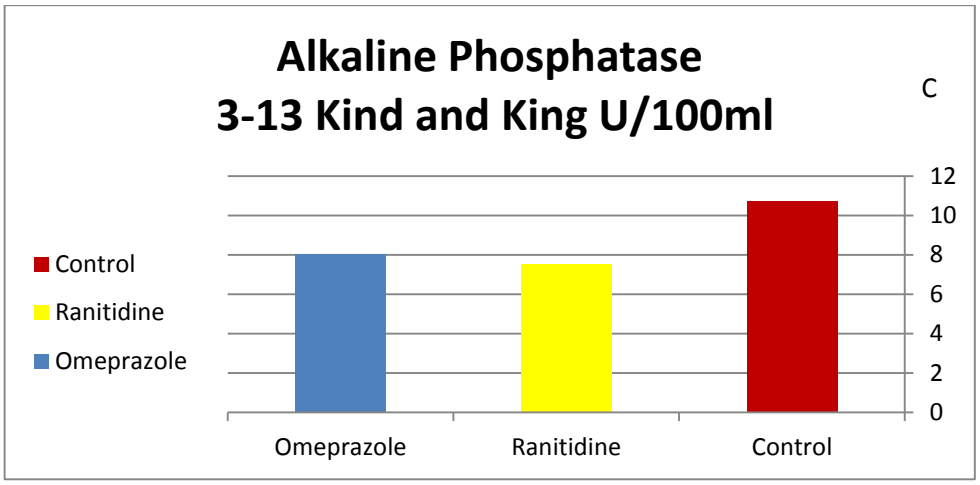

Chart 3: Effect of ranitidine and omeprazole compared with control on level of serum alkaline phosphatase in the body.

Total Serum Protein:

The results showed that there are significant differences P≤0.05 in the level of total protein among those who are taking anti-ulcer drugs, compared with healthy people, the study showed a decrease in the level of total protein compared with healthy people this is due toProlonged use causes liver cirrhosis Which leads to a decrease in the amount of total protein.[29][30]

Table 4: Effect of ranitidine and omeprazole compared with control on level of total serum protein in the body.

Parameter		Number	mean±SD
Total serum Protein	Control	35	77.7437±5.47345
	Ranitidine	35	52.4621±11.29795
	Omeprazole	35	53.5736±9.97103

There is a significant difference (P≤0.05)

Total Serum Protein Level

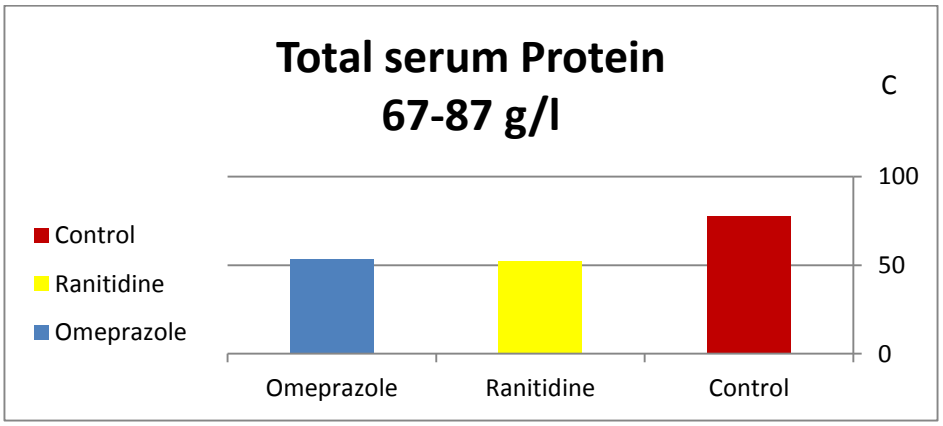

Chart 4: Effect of ranitidine and omeprazole compared with control on level of total serum protein in the body.

Total Serum Bilirubin

The study showed when that there are significant differences in the level of Total serum Bilirubin, for those who are taking anti-ulcer drugs compared with healthy people p≤0.05, the study showed a slight increase in the level of Total serum Bilirubin, compared with healthy people. This is due to the effect of the drug on the liver and this is agrees with (Yara Cavalcante et al, 2005)[31].

The study also showed no significant differences in the level of Total serum Bilirubin users between these drugs and the like-that between them on the liver to influence[29][30].

Table 4: Effect of ranitidine and omeprazole compared with control on level of total serum Bilirubin in the body.

Parameter		Number	mean±SD
Total Serum Bilirubin	Control	35	0.6656±0.19111
	Ranitidine	35	1.0071±0.41780
	Omeprazole	35	0.8553±0.45817

There is a significant difference (P≤0.05)

Total Serum Bilirubin level

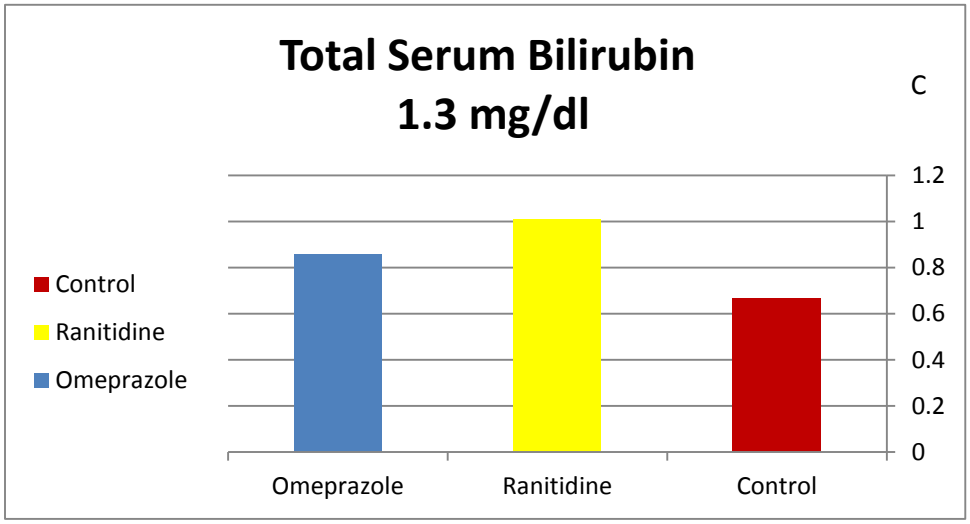

Chart 5: Effect of ranitidine and omeprazole compared with control on level of total serum Bilirubin in the body.

References

1- Kong F, Singh RP, "Disintegration of solid foods in human stomach". J. Food Sci. 73 (5) (June 2008). : P67–80.

2- Sherwood, Lauralee, Human physiology: from cells to systems. Belmont, CA: Wadsworth Pub. Co. (1997).P.50-60

3- Najm, W, "Peptic ulcer disease.". Primary care 38 [3] (September 2011): 383–94.

4- Milosavljevic, T; Kostić-Milosavljević, M; Jovanović, I; Krstić, M, "Complications of peptic ulcer disease.".Digestive diseases (Basel, Switzerland) 29[5] (2011): P.491–3.

5- The American Society of Health-System Pharmacists, "Ranitidine". Retrieved Dec 1, 2015.

6- Fedorowicz, Z; van Zuuren, EJ; Hu, N, "Histamine H2-receptor antagonists for urticaria.". The Cochrane database of systematic reviews 312,(14 March 2012).

7- Clark, K.; Lam, L. T.; Gibson, S.; Currow, D, "The effect of ranitidine versus proton pump inhibitors on gastric secretions: a meta-analysis of randomised control trials".Anaesthesia 64. (2009): P.652–657.

8- The American Society of Health-System Pharmacists, "Omeprazole". Retrieved Dec 1, 2015.

9- "DrugBank: Omeprazole (DB00338)". Drugbank.ca. Retrieved 2014-02-24.

10- Trauner M, Boyer JL, Bile salt transporters: molecular characterization, function, and regulation. Physiol Rev 83(2003):P.633,

11- Marshall, W.J.and Bangert, S.K. Clinical chemistry. 6th ed. Edinburgh: Mosby; 2008.

12- Pagana, K.D.and Pagana, T.J. Manual of diagnostic and laboratory tests. 4thED. St. Louis,USA: Mosby; 2010.

13- Fischbach, F.T.; Dunning, M.B.; Taylor, C.; Lillis, C.and LeMone, P. A manual of laboratory and diagnostic tests. 8thED. Philadelphia, USA: Lippincott Williams and Wilkins; 2008.p.317-321.

14- Oyaizu, M. Studies on products of browning reaction: Antioxidativeactivities of product6s of browning reaction prepared from glucosamine. Jp.n J. Nutr. 1986; 44:P 307 – 315.

15- Hui, M. and Tenenbaum, H.C. New face of an old enzyme: alkaline phosphatase may contribute to human tissue aging by inducing tissue hardening and calcification. Anat. Rec. 1998;253: 91-94.

16- Kosasa, T.S., "Measurement of Human Luteinizing Hormone." J. Reprod. Med. 1981; 26 :P. 201-6.

17- Guyton & Hall, Medical Physiology, Gastointestinal physiology, Unit XII, 11th , Elsevier Saunders, 2006, P.791.

18- Devlin,T. M. (2002). Text Book of Biochemistry. 5th. ed., Wiley–Liss,Inc publication. Philadelphia .P (98 -154).

19- Stocker, R; Yamamoto, Y; McDonagh, A.; Glazer, A.; Ames, B. "Bilirubin is an antioxidant of possible physiological importance" Science 235 (1987). (4792):1043, P.6.

20- Baranano, D. E.; Rao, M.; Ferris, C. D.; Snyder, S. H. "Biliverdin reductase: A major physiologic cytoprotectant Proceedings of the National Academy of Sciences 99 [25] (2002): 16093, P.8.

21- Sedlak, T. W.; Saleh, M.; Higginson, D. S.; Paul, B. D.; Juluri, K. R.; Snyder, S. H.."Bilirubin and glutathione have complementary antioxidant and cytoprotective rolesProceedings of the National Academy of Sciences 106 (2009) [13]: 5171, P.6.

22- Liu, Y; Li, P; Lu, J; Xiong, W; Oger, J; Tetzlaff, W; Cynader, M."Bilirubin possesses powerful immunomodulatory activity and suppresses experimental autoimmune encephalomyelitis Journal of Immunology 181 (3) (2008)*:* 1887, P.97.

23- Scherwin E, Kaplan, L.A., pesce, A. J, Kaz-mierc-zaks: liver function clinical chemistry Ttheeory Analysis , Correlation , 4th ed. s.c., (mosby Inc. eds. St Louis USA), (2003), 492.

24- Young D: Effects of preanalyical variables on clinical laboratory tests 2nd edition, .(1997),

25- KIND P.R.and king , E. J, Estimation of Plasma Phosphatase by determination of hydrolysed phenol with amino- antipyrine-, J. Clin. Path. 1954; 7, P.322-6

26- Tietz, N. W., "Text Book Of Clinical Chemistry", 3rd Edition, C. A. Burits, E. R. Ashwood, W.B. Saunders Company, (1999), pp. 477-530, 668-672, 826-835, 1241-1245.

27- Ramrakhiani S, Brunt EM, Bacon BR. Possible cholestatic injury from ranitidine with a review of the literature. Am J Gastroenterol 1998; 93:P. 822-6.

28- Jochem V, Kirkpatrick R, Greenson J, Brogan M, Sturgis T, Cook-Glenn C. Fulminant hepatic failure related to omeprazole. Am J Gastroenterol 1992; 87: P.523-5.

29- Middle East Medical Index,Glaxosmithkline pharma, Section 5, 30th ed, January 2009, actavis creating value in pharmaceuticals. P740-741.

30- Middle East Medical Index, Hikma, Section 5, 30th ed, January 2009, actavis creating value in pharmaceuticals. P740-741.

31- Yara Cavalcante Fortes Goulart, Vania Ramos Sela, Simoni Obici, Juliana Vanessa Colombo Martins, Fernanda Otobone, Diogenes Aparicio Cortez and Elisabeth Aparecida Audi, (Evaluation of Gastric Anti-ulcer Activity in a Hydroethanolic Extract from Kielmeyera coriacea) Departamento de Farmácia e Farmacologia; Universidade Estadual de Maringá 2005; Av. Colombo