ISSN: 1991-8941

Study of photolysis on the active material Phenylbutazone in veterinarian drug Isophen

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Received: 5/1/2012 Accepted:9/5/2012

Abstract:

The veterinary medicine isophen was used in this study. Isophen contains phenylbutazone as active material .Numbers of samples of isophen were prepared and were determined absorbance were determined and comparison subjected to radiation for different periods (1 ,2, 3, 4, 5) hrs. the Maximum absorbance were determined and compression Maximum absorbance's Study are performed. And ensure that the impact of irradiation on the active ingredient in the medication. The results reveal that has been reached that there is significant impact of irradiation as well as the time of irradiation on the decomposition of the active ingredient in the medication was found that with the continuation of the time of irradiation increases decomposition.

Key words: Isophen, Phenylbutazone, photolysis

Introduction:

Phenylbutazone is an effective non- steroidal anti-inflammatory drug (NSAID) with antipyretic and analgesic activity , used in veterinary medicin for mor than 50 years to treat bone and joint inflammations laminitis and inflammation of soft tissues [1] . It is widely used in doges and horeses but because of toxicity and the lack of established maximum residue limit , is not approved for use in food producing animals . The most serious adverse reaction of phenylbutazon observed in human and animals are : gastric and intestinal ulc eration and bleeding, disturbances in platelet function.

The prolongation of gestation or spontaneous labour and Changes in renal function . In Finland phenylbutazon has been on of the most widely used non- steroidal anti-inflammatory drug after acetyl salicylic acid . There is still no maximum residue level for phenylbutazon at the 1998. [2] phenylbutazon effects by preventing the synthesis of prostaglandins . As a medicine phenylbutazon has antipyretic , analgetic and anti-inflammetoric effects oxyphenbutazon a metabolic of phenylbutazon has one fifth of the medical activity of phenylbutazon [1, 3].

Mechanism of action

Inhibition of the arachidonic acid gas cade at the level of prostaglandin H syntheses and prostaglandin syntheses results in decrease production of prostaglandins and thromboxane.

also Inhibits urate crystal phagocytosis by synoviocytosis [4]. Phenylbutazon

Distribution : phenylbutazon is distributed mainly in to plasma and extra celluler fluid , as indicated by the relatively small volume of distribution , this is low volume of distribution is also indicative of only no minal tissue binding [5].

Pharmacokinetics: phenylbutazon is absorbed from both the stomach and small intestine . the drug is distributed through out the body with highest levels attained in the liver , heart , Lungs, kidneys , and blood . Both phenylbutazon and oxyphenylbutazon cross the placenta and are excrete d into milk [5].

Adverse effect / wornings.

The primary concernt with phenylbutazon therapy in humans include its bone marrow effects (agranulo cytosis, aplastics anemia) renal and cardiovascular effects (fluid retention to acute renal failure)[5].

Dosage and administration:

phenylbutazon may be administred orally (via paste, powder , or feed- in) or intravenously. It should not be given intramuscularly or injected in any place other than a vein , as it can cause tissue damage.

Side effect and disadvantages of phenylbutazon :

Side effect of phenylbutazon are similar to that of the Non-steroidal anti-inflammatory drugs overdos or prolonged use Can cause gastrointestinal ulcers, blood dyscrasia ,kidney damage.Phenylbutazon Is abtaind in straight forward manner by Condensation of diethyl-n-butylmalonate with hydrazobenzen in the presence of base.In effect ,this represent the

formation of heterocyclic system by simple Lactamization [6] phenylbutazon should be used cautiously in
pregnant or nursing mares ,as it may be toxic to the embryo and can be transferred via the umbilical cord and milk.

High dose of phenylbutazon may be considered arules violation under some equestrian organization as the drug may remain in the blood stream four to five days after administration . In human phenylbutazon is very dangerous as it can cause aplastic anemia .The medicine should be give i n apast from to avoid contact with the medicin .Never breathe powder from crushing tablets.

Methods:

The drug used in this investigation was Isophen and the active material in this medicine is Phenylebutazone which is applied as Injected solution of 200 ml samples was prepared according to the following steps 1- 5ml of drug was dissolved in ethanol as solvent
2- No. of samples were prepared and subjected to radiation for different Periods (1,2,3,4,5) hours
3- Absorbances was measured using spectrophotometer and λmax was termine
4- differences between the values of λmax for all samples was recorded .

Result and Discussion:

Many authors [3,6,7] observed degradation of Penyle butazone During analysis , if samples were exposed to acidic condition ,left Dry and open to the atmosphere ,or when containing oxygen ,diethyl ether was used as elution solvent in solid – phase extraction . our experiences indicate that addition of ascorbic acid solution as stabilizer to the extract . Aroom temperature , photochemical spectrophotometric method has been developed for the assay of Phenyle butazone and its degradation products are reported as well as irradiation times (1-5) hrs. which correspond to maximum ultra violet signals of photo products. Our study investigate that the results of samples radiation for different Periods (1,2,3,4,5) hours showed a lowering in λ_{max} values with Increasing of time radiation also absorbance increased , as shown In table (1) and figures. (1-6).

Table (1): λ_{max} (nm) for isophen at different time of radiation .

No.	Radiation time (hrs .)	λ_{max} (nm)
1	Pure	280
2	1	278
3	2	277
4	3	275
5	4	273
6	5	272

Studies of oxygenation of phenyle butazone have established that phenyle butazone is true reducing cofactor for peroxidase activity of prostaglandin H synthase [6,8,9] oxidized Phenyle butazone incorporates molecular oxygen to yield 4-hydroperoxy - Phenyle butazone which then reduced to 4- hydroxy- Phenyle butazone [10] , these observation have been used to support the mechanism [8] . shown in scheme (1) , table (2).

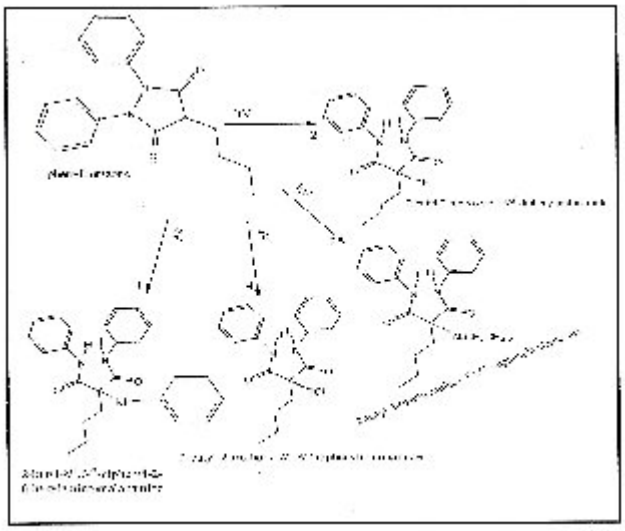

Table (**2**): products of mechanism of photolysis for phenylbutazone

No	hV → Products	
1	R=NHPh	2-butyl-N1,N3-diphenyl-2-(phenylamino)malonamide
2	R=OH	2-butyl-2-hydroxy-N1,N3-diphenylmalonamide
3	R= $N(CH_2CH_3)_2$	2-butyl-2-(diethylamino) N1,N3-diphenylmalonamide
4	R= OCH_3	2-butyl-2-methoxy-N1,N3-diphenylmalonamide

The malonamide in no. 1 when (R= NHph) and No.2 when (R= OH) And the 2-oxohexanamide in No.5 . when the solutions was basified With diethyl amine . The amino diamid in no. 3 when (R= N(Et)2) was Produced in addition to No.2 when (R= OH) and No. 2 . In methanol Solution the malonamide in No. 1 when (R= NHph) and No. 4 when (R= OMe) where obtained .

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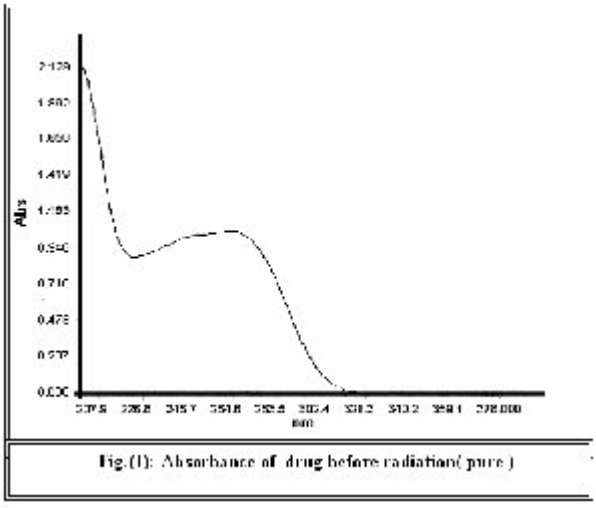

Fig.(1): Absorbance of drug before radiation(pure)

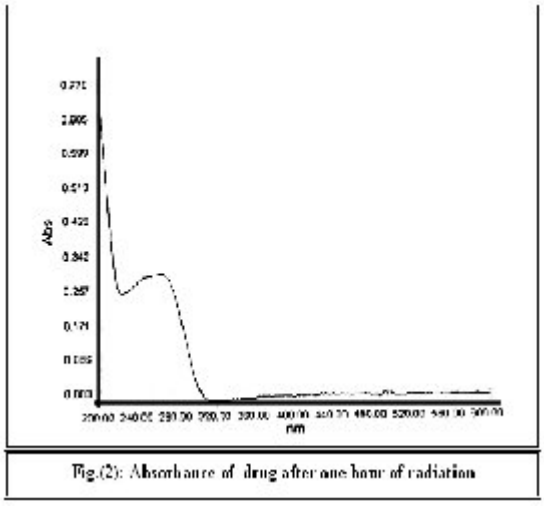

Fig.(2): Absorbance of drug after one hour of radiation

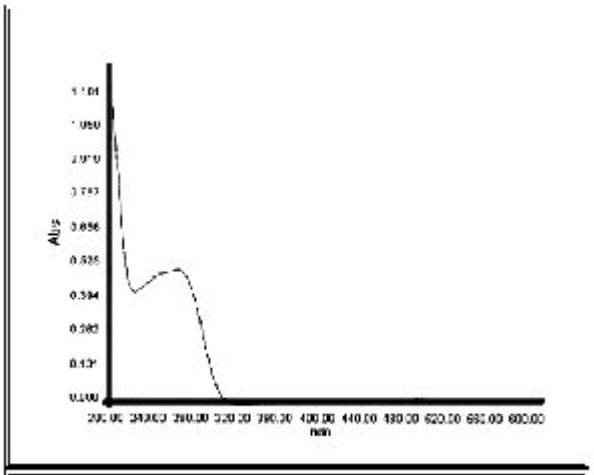

Fig.(3): Absorbance of drug after two hour of radiation

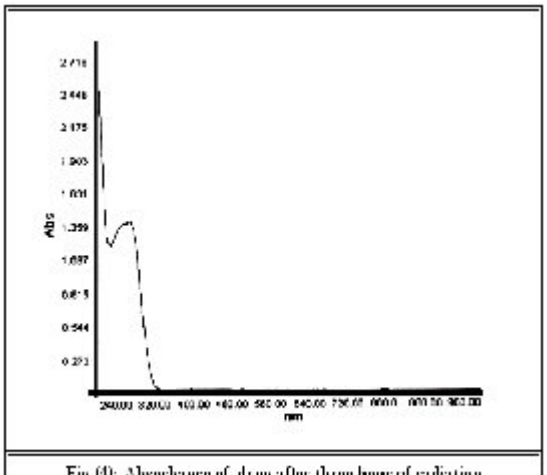

Fig.(4): Absorbance of drug after three hour of radiation

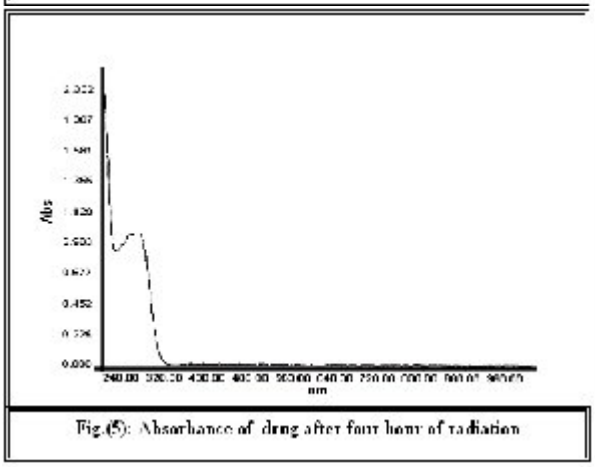

Fig.(5): Absorbance of drug after four hour of radiation

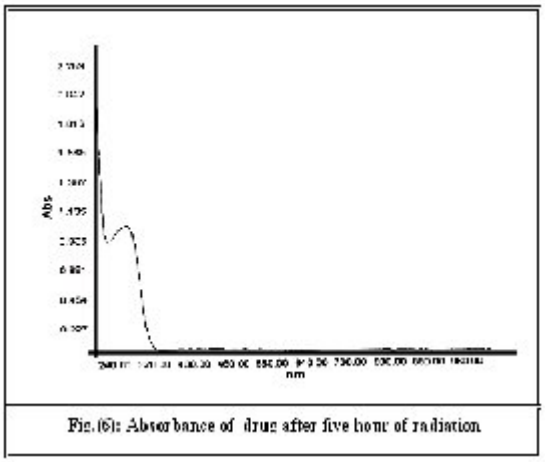

Fig.(6): Absorbance of drug after five hour of radiation

دراسة التحلل الضوئي للمادة الفعالة Phenylbutazone في الدواء البيطريIsophen

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الخلاصة:

أستخدم في هذا البحث الدواء البيطري آيزوفين Isophen الحاوي على المادة الفعالة فنيل بيوتازون Phenylbutazone إذ تم تحضير عدد من النماذج للدواء البيطري المذكور ثم عرضت النماذج المحضرة للتشعيع ولفترات زمنية مختلفة (1 ,2, 3, 4, 5) ساعة ثم حسبت الامتصاصية العظمى (λ max) لكل نموذج بعد التشعيع لغرض دراسة المقارنة بين القيم العظمى للامتصاصية لجميع النماذج المحضرة من الدواء آيزوفين والتأكد من تأثير فترة التشعيع على المادة الفعالة في الدواء . حيث بينت النتائج التي تم التوصل إليها انه يوجد تأثير كبير للتشعيع وكذلك الفترة الزمنية للتشعيع على تحلل المادة الفعالة في الدواء إذ وجد انه مع استمرار فترة التشعيع تزداد نسبة التحلل.