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

Hanan H. Flaeh     Wajeeh Y. Mohammed      Authman S. Ibrahim    Sattar  S. Ibrahim
University of Anbar - College of Science
Received: 5/1/2012    Accepted: 9/8/2012

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 medicine for more than 50 years to treat bone and joint inflammations laminitis and inflammation of soft tissues [1]. It is widely used in dogs and horses 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 phenylbutazone observed in human and animals are: gastric and intestinal ulceration and bleeding, disturbances in platelet function. The prolongation of gestation or spontaneous labour and Changes in renal function. In Finland phenylbutazone 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 phenylbutazone at the 1998. [2] Phenylbutazone effects by preventing the synthesis of prostaglandins. As a medicine phenylbutazone has antipyretic, analgetic and anti-inflammmtoric effects oxyphenbutazone a metabolic of phenylbutazone has one fifth of the medical activity of phenylbutazone [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 synoviocytes [4]. Phenylbutazone

Distribution: phenylbutazone is distributed mainly in to plasma and extra cellular 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: phenylbutazone 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 phenylbutazone and oxyphenbutazone cross the placenta and are excreted into milk [5].

Adverse effect / warnings.
The primary concern with phenylbutazone 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:
phenylbutazone may be administred orally (via paste, powder, or feed-in) or intravenously. It should not be given intramuscularly or injected in any other place other than a vein, as it can cause tissue damage.

Side effect and disadvantages of phenylbutazone:
Side effect of phenylbutazone are similar to that of the Non-steroidal anti-inflammatory drugs overdose 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 a rules violation under some equestrian organization as the drug may remain in the bloodstream four to five days after administration. In human phenylbutazon is very dangerous as it can cause aplastic anemia. The medicine should be given in past from to avoid contact with the medication. 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 $\lambda_{max}$ was termine
4- differences between the values of $\lambda_{max}$ for all samples was recorded.

Result and Discussion:
Many authors [3,6,7] observed degradation of Phenyle 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. At room 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 $\lambda_{max}$ values with increasing of time radiation also absorbance increased, as shown in table (1) and figures. (1-6).

<table>
<thead>
<tr>
<th>No.</th>
<th>Radiation time (hrs.)</th>
<th>$\lambda_{max}$ (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pure</td>
<td>280</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>278</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>277</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>275</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>273</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>272</td>
</tr>
</tbody>
</table>

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).
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) were obtained.

References:

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

<table>
<thead>
<tr>
<th>N°</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2-furyl-N,N,N,3-diphenyl-2-phenylamino malonamide</td>
</tr>
<tr>
<td>2</td>
<td>2-furyl-N,N,N,3-diphenyl-2-phenylamino malonamide</td>
</tr>
<tr>
<td>3</td>
<td>2-furyl-2-(diethylamino)-N,N,N,3-diphenyl malonamide</td>
</tr>
<tr>
<td>4</td>
<td>2-furyl-2-methoxy-N,N,N,3-diphenyl malonamide</td>
</tr>
</tbody>
</table>

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

Fig. (2): Absorbance of drug after one hour of radiation
دراسة التحلل الضوئي للمادة الفعالة في الدواء البيطري Phenylbutazone

حنان حسن قلبي
 وجهي يونس محمد
 عمران سالم إبراهيم
 ستار سالم إبراهيم

E-mail: scianb@gmail.com

الخلاصة:

استخدم في هذا البحث الدواء البيطري أيسوفين Isophen الحاوي على المادة الفعالة فيل بروتازون Phenylbutazone، إذ تم تحضير عدد من النماذج للدواء البيطري المذكور ثم عرضت النماذج المحترمة للتشعيب بفترات زمنية مختارة (1، 2، 3، 4، 5) ساعة ثم حسبت الامتصاصية العظمى (λmax) لكل نموذج بعد التشعيب وعرض دراسة المقارنة بين القيم العظمى للامتصاصية لجميع النماذج المحترمة من الدواء أيسوفين. وتأكد من تأثير فترة التشعيب على المادة الفعالة في الدواء. حيث بينت النتائج التي تم التوصل إليها أنه يوجد تأثير كبير للتشعيب وكذلك الفترة الزمنية للتشعيب على تحلل المادة الفعالة في الدواء إذ وجد أنه مع استمرار فترة التشعيب تزداد نسبة التحلل.