Iraqi Journal of Industrial Research, Vol. 9, No. 1 (2022)

Open Access

Iraqi Journal of Industrial Research (IJOIR)

Journal homepage: http://ijoir.gov.iq

Formulation of Neomycin Sulphate 0.35 %(w/v) & Hydrocortisone 0.5% Otic Drop

Muhammad Jassim Muhammad*, Awatif I. Muhammed, Haneen Muhammad Jassim

Veterinary Drugs Researches and Production Center/ Corporation of Research and Industrial Development – Iraq

Article information

Article history:
Received: January, 27, 2022
Accepted: April, 25, 2022
Available online: June, 14, 2022

Keywords:
Hydrocortisone,
Neomycin sulfate,
Ear drops

***Corresponding Author:**
Muhammad Jassim Muhammad
Mohammedgasem11@yahoo.com

DOI:
https://doi.org/10.53523/ijoirVol9I1ID154

Abstract

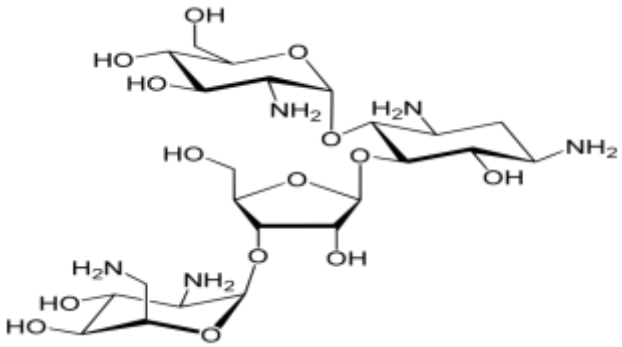
Neomycin sulfate and hydrocortisone ear drops of veterinary pharmaceuticals used as an antibiotic and ant inflammatory to treat infections caused by bacterial infections in the middle ear of large and small field animals caused by gram positive and negative bacteria like, *Staphylococcus aureus*, *Escherichia coli*, *Homophiles influenza*, *Klebsiella–Enterobacter* species, *Neisseria species*, and *Pseudomonas aeruginosa*. The action of mechanism neomycin sulfate is inhibition of protein synthesis in bacteria cell which is lead to kill the bacteria and the action of hydrocortisone is ant inflammation in the infected area in animals. In order for this preparation to be researched and applied, several primary pharmaceutical preparations were prepared until the final and stable structure was reached. The amount of the active substance at room temperature was 100%. This activity is good and within the permissible limits According to the veterinary constitutions [90-110].This process involved several stages of collecting information in the materials involved in the formulation and from effective and added materials And then the preparation of the composition according to the international pharmaceutical specifications using the constitutions of the drug followed by the study of stability and resistance to the product temperature room and then send samples for field examination Department of Veterinary, was used in the treatment of cases of bacterial infections of the middle ear infections in cats use 3 or 4 drops in the affected ear three or four times for 3-5 days and results came very good according the clinical evaluation.

1. Introduction

Neomycin sulfate and hydrocortisone drops for the middle ear are very important preparations in the treatment of middle ear infections. Otitis is the definition of the ear canal and/or the pinna. Otitis externa is a term used in the external canal only, outside the tympanic membrane. When it comes to the eardrum and the tympanic vertebra, the term otitis media is used. Otitis media means damage to the hearing organ; Usually it would be Neurological symptoms and deafness are present [Kennis, 2013]. Otitis is seen in first opinion veterinary practice on a regular basis, representing some 10-20% of all canine cases presenting to practitioners. Otitis externa (OE) (inflammation of the external ear canal, or EEC) is typically complicated by secondary infection which can – along with other factors – lead to rupture of the tympanic membrane (TM) and the development of otitis media (OM). Over 50%

of dogs presenting with chronic OE have concurrent OM [Hannah lipscomb&Filippo De bellis2021]. Otitis media, an inflammatory disease of the middle ear cavity that is common in dogs, secondary otitis media occurs in about 16% of acute otitis media and in up to 50% to 80% of chronic otitis media [Cole L. K., 1998; Little *et al*., 1991]. In the cat, otitis can be a challenging clinical problem because the approach The most common clinical and treatment of otitis media rarely leads to satisfactory results when applied to cats [Kennis, 2013]. Sore throat extrinsic exotropia, the beginning, the beginning at the beginning to the temperature of the outer, the outer, the outward, the outer beginning of the external duct. Therefore, it can a wide range of clinical signs occur, including head shaking, ear scratching, auricular (ceramic or purulent) discharge (including otic hematoma and acute moist dermatitis near the base of the ear), swelling and pain as well as trauma, disturbances, and malnutrition [Rosser, 2004]. In cases of recurrent or chronic otitis externa, clinical signs may progress to include changes in the external ear canal and the tympanum is more likely to rupture and progress of concurrent otitis media [Rosser, 2004]. Overseas may occur more commonly in a cat than a dog. It is usually a one-sided problem, but may be bilateral [Kennis, 2013]. Clinical signs may include head shaking or putting feet in the ears and severe cases, cats may show head tilting to the affected side. In dogs, otitis media are frequently associated with chronic otitis, media resulting in damage to the tympanic membrane. Usually diagnosed Otitis media during ear examination. The tympanic membrane may appear to swell outward. Fluid and air bubbles can be seen behind the intact tympanum [Kennis, 2013]. Otitis media should also be considered when a veterinarian examines an animal with a differential diagnosis of otitis media or a neurological disease affecting the head, including vestibular disease, Horner syndrome, or facial nerve damage, Horner's syndrome, or facial nerve damage [Gotthelf, 2004]. Many topical ear treatments are available on the market, but most contain a weak or moderate corticoid (Prednisolone or hydrocortisone). [Germania, 2008; Morris, 2004] An antibiotic belonging to the group of aminoglycosides belonging to the streptomycin family. It is a white to yellowish powder that dissolves quickly in water and has a broad spectrum action against Gram-negative bacteria such as *Salmonella*, *Proteus*, *klebsiella*, *E. coli*, and *Entrobacter*.

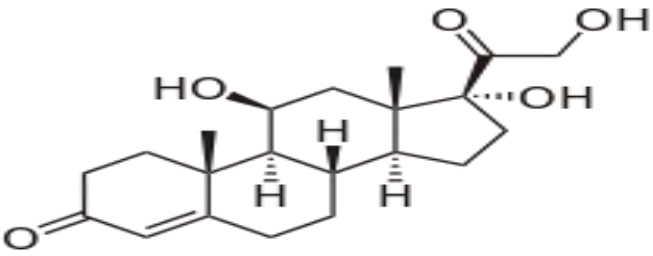
Neomycin and hydrocortisone suspension as ear drops are used to treat antibacterial infections and ant inflammation in animals. It consists of two main substances: Neomycin sulfate neomycin sulfate is a widely used aminoglycoside antibiotic with good inhibitory activity against gram-negative and some gram-positive bacterial infections in animals. Neomycin sulfate specifically targets a conserved sequence of 16S ribosomal RNA and interferes with protein synthesis by transporting into the cytoplasm of bacteria [Becker & Cooper, 2013]. Mechanism of action - Neomycin kills and inhibits the action of the bacterial cell by preventing the formation of the bacterial cell wall by preventing the binding of transpeptidation to peptoglycol, which is the main component of the bacterial cell wall, thus increasing the activity of enzymes degrading the cell wall by a process known as hydrolases nureintolysins [Leigh Ann 2015, Sanjai Sinha, 2016].



Mw= 615.629 g/mol **s $C_{23}H_{47}N_5O_{18}$**

Figure (1). The chemical structure of neomycin sulfate compound.

Hydrocortisone Hydrocortisone was discovered in 1955. It is on the WHO's List of Essential Medicines, the most effective and safe medicines needed in a health system. [Somerset, NJ., Solu-Cortef, 2016] It is available as an alternative treatment. The mechanism of action of hydrocortisone lies in reducing the secretion of these substances and limiting the transmission of multinucleated white blood cells to the affected site, in addition to reducing capillary permeability.



MW= 362.460 g/mol **$C_{21}H_{30}O_5$**

Figure (2). The chemical composition of hydrocortisone.

The microbiological examination was carried out in the laboratory of our center and the acceptance certificate was obtained by the above center. Other forms were also sent for the purpose of conducting the field, evaluation and the results were good and the acceptance certificate was obtained by the veterinary department of the veterinary hospital Theoretical Part This optional section should be used only if more extensive theoretical derivations are needed. Simpler theories and methods should be a part of either Introduction or Experiment, respectively. All equations, including those describing chemical reactions, must be written in separate lines and numbered. The symbols of quantities should be explained immediately below the equation if they were used for the first time. Theoretical part should be Times New Roman, justified, regular; font size: 11 single. If you have any figures or tables in this section, please use the same format that will be mentioned in the "Results and discussion" part.

2. Experimental Procedure

Raw materials and devices use: Raw materials are hydrocortisone, Neomycin sulfate, Sod. EDTA, glycerin, additives.

Devices used: are Magnetic starrier hot plate (Germany), Mixer for liquids (Germany), Heater (Turkey), Sensitive Balance (Germany).

Procedure: Weighing the raw materials and ingredients by the quantities indicated for each of them to prepare 100 g.

Prepare of 100 g of the drops:

1. Add 30 ml of distilled water into a dry glass beaker (250 ml) with the addition of neomycin sulphate, boric acid, sod. EDTA with continuous mixing with magnetic front.
2. The weight of hydrocortisone was added to it glycerin ml with the addition of water in a little way, mixed with magnetic sterior, and the active substance was added in small quantities and gradual.
3. Step No. (2) Is added to step No. (1) With continuous mixing.
4. Mix well and add to the mixture.
5. The formula is then placed in a 10ml opaque container.
6. Measuring the acidity rate (PH=2-4.5)
7. Samples for biological analysis were sent.
8. Forms were sent for field evaluation.

3. Results and Discussion

The results of the microbiological examination show the effectiveness of the preparation from a biological point of view, and this was confirmed by the results of the examination in the microbiological laboratory at the

Veterinary Drugs Research and Production Center, where its effectiveness was 97% and it is within the veterinary department 90-110%. A stable and stable composition was obtained by studying the stability at room temperature with a degree of 40℃ and for a period of 3 months, as it was noted that the effectiveness of the preparation was not affected by the passage of time, as it was noted that the effectiveness decreased to 91% at a temperature of 60℃ This is due to exposing the product to harsh conditions for a period of 3 months, but within the constitutionally permissible limits [90-110%] because the effectiveness of hydrocortisone and neomycin remained within the permissible limits and the decrease in effectiveness was limited, and this indicates the stability and effectiveness of the drug combination. The field examination also showed its therapeutic efficacy in cases of bacterial infection affecting the outer and middle ear pinna in and field animals. And the composition obtained a certificate of acceptance from the veterinary department/ veterinary hospital.

Stability study:

The stability of the product was monitored at room temperature for a period of 3 months, according to the listed results. The initial evaluation was time zero (97%).

Table (1). Stability study at temperatures (50, 40, 60℃).

Active ingredient Neomycin, Hydrocortisone Humidity%			Follow	No
60▫c,75%	50▫c,65%	40▫c 60%		
95%	95%	97%	After 1 month	١
90%	95%	97%	After 2 months	2
91%	93%	97%	After 3 months	3

Table (2). Concentration of Hydrocortisone & neomycin sulfate at zero time.

NO.	Subject	Concentration (%)
1	Hydrocortisone	97%
2	Neomycin sulfate	95%

Table (3). Physical specifications of the formula.

Analysis time	PH	Color	Homogenization
Zero time	4.2	White	homogenized
After one month	4.2	White	homogenized
After two month	4	White	homogenized
After three months	3.8	White	homogenized

4. Conclusions

We conclude from the results that the physical and chemical specifications of the final formula were fixed during the period of the stability study. It is recommended to use the preparation as a new product, after reviewing the results of the biological analysis and field evaluation after testing it on animals (cats and dogs) in cases of bacterial infections of the outer and middle ear, as it gave fruitful results in the work.

References

[1] Hannah Lipscmb and Filippo De Bellis,"A diagnostic approach to canine otitis*" vetfocus royalcanin.com* / en, issue number 31.2, 2021.

[2] L. K. Cole, J. KOWLSKI J., and A. Hiller, "microbial flora and antimicrobial sensitivity patterns of isolated pathogens from the horizontal ear canal and middle ear in dogs with otitis media", *Journal of the American veterinary medical association*, vol. 212, pp. 534-538, 1998.

[3] L-N. Gotthalf, "diagnosis and treatment of otitis media in dogs and cats", *Vet Clin North Am small Anim Pract"*, vol. 34, pp. 469-487, 2004.

[4] Germain, P. A. C. E., and E. Bensignor, "Comparison of two topical remedies in treating otitis", 2008.
[5] R. A. Kennis, "Feline otitis: diagnosis and treatment", *vet clin North Am small Anim pract*, vol. 43, pp. 51-56, 2013.
[6] E. J., Jr, Rosser, "Causes of otitis externa", *Vet Clin North Am small anim pract*, vol. 34, pp. 459-468, 2004.
[7] D. O. Moris, "Medical therapy otitis externa and otitis media', *Vet Clin North Am small Anim pract*, vol. 34, pp. 541-555, 2004.
[8] Leigh Ann Anderson, Sanjai Sinha and MD, "Hydrocortisone *Drugs.com*", *American Society of Health-System Pharmacists*", February 9, 2015. 20 September, 30 August 2016.
[9] NJ. Somerset, Solu-Cortef, "Pfizer U.S September Pharmaceuticals Group, New York, NY Hydrocortisone" *Drugs.com*., vol. 20, pp. 1, 2016.
[10] WHO, 13,8, "Model List of Essential Medicines (19th List)" (PDF), December 2016. World Health Organization, April 2015.
[11] Sr. R. J. Lewis, Hawley's, John Wiley & Sons, "Chemical Dictionary". New York, 14th Edition, p. 585. 2001.
[12] M. D. Rockville, Allen LV Jr, *USP Pharmacopeia Convention, Inc. USP Pharmacists' Pharmacopeia. 2nd ed.: US Pharmacopeia Convention*, Inc., pp. 189,197-198, 255, 288, 764- 765, 2, 2005.
[13] Akaike N., Harata Nperforated, "Patch recording and its applications to analyses of intracellular mechanisms Jpn. J. physiol, Nystatin", vol.44, no. 5, pp. 433-73, 1994.
[14] Alexander logmanbook shop/London NY, "An introduction to veterinary pharmacology", 4TH edition pp. 325-318, 1985.
[15] British pharmacopeia, "specific monograph", vol. 3, London SW85NQ, 5th edition, 2013.
[16] British pharmacopeia part 6 book (Veterinary), London the stationary office, pp. 647, 2019.
[17] B. Becker, M. A. Cooper, "Aminoglycoside antibiotics in the 21st century ACS Chemical Biology", vol. 8, pp. 105-115. 2013.