



## Formulation of Nystatin 2.4%, Neomycin Sulfate 0.35%, Dexamethasone 0.05% (w/w) Ointment

<sup>1</sup>Muhammed J. Muhammad\*, <sup>1</sup>Ferial M. Mahdi, <sup>2</sup>Haneen M. Jassim

<sup>1</sup>Veterinary Drugs Researches and Production Center/ Corporation of Research & Industrial Development – Iraq

<sup>2</sup>Al-Razi Center for Research & Medical Kits Production/ Corporation of Research & Industrial Development – Iraq

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#### \*Corresponding Author:

Muhammed J. Muhammad

[mohammedgasem980@gmail.com](mailto:mohammedgasem980@gmail.com)

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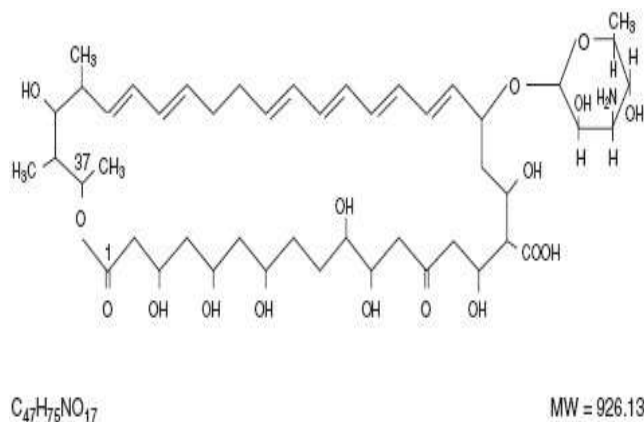
### Abstract

The aim of study is production of new local drug consisting of Nystatin, Neomycin sulfate, Dexamethasone ointment are veterinary medicinal preparations used in the treatment of exogenous fungi and infections in small and large animals that cause by (*candida albicans*) and affected by gram positive and gram negative bacteria like (*Staphylococcus aureus*, *Escherichia coli*, *Haemophilus influenza*, *Klebsiella-Enterobacter species*, *Neisseria species*, and *Pseudomonas aeruginosa*). Nystatin is considered one of the safe drugs when treating external fungal infections in field animals. Neomycin works by inhibiting protein synthesis in the bacterial cell and thus leads to the killing of bacteria either dexamethasone works to stop infections in the affected area of animals. In order for this product to be both research and applied, many of the initial pharmaceutical compositions were prepared until the final and stable composition was reached in this form. (90-110% permissible limit of activity). This process included several stages of collecting information on the substances included in the formula, active substances and additives, and then preparing the formula according to the specifications. International pharmacology using pharmacopoeia, followed by a study of stability and resistance of the preparation at room temperatures, then sending samples for field examination to the veterinary department and for the lack of cases for other animals where it was used on cases of fungal infections and skin infections in small animals (Cats). The treatment period was 5-10 days, and it brought very good results, according to the field evaluation form attached to the research. Outcomes of study its good and new research and very important to treatment skin infection in small animals.

### 1. Introduction

Nystatin, Neomycin sulfate, Dexamethasone ointment are very important preparations in the treatment of cases infected with external fungi such as Candidiasis caused in particular [*candidiasis albicans*] or any fungus of the family of *candida* genus [Psychia], which causes various infections ranging from superficial infection limited on

the skin or on the mucous membranes [1], where it has an important role in skin and subcutaneous infections in dogs, cats and birds [2] and skin infections caused by gram-positive and gram-negative bacteria such as *Staphylococcus aureus*, *Escherichia coli*, *Haemophilus influenzae*, *Klebsiella-Enterobacter species*, *Neisseria species*, and *Pseudomonas aeruginosa* [3].



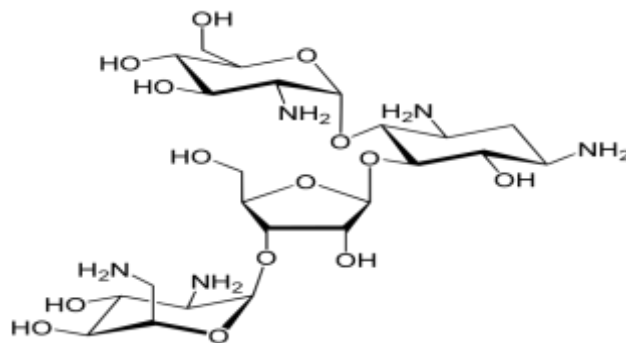
**Figure (1).** Chemical structure of Nystatin [4].

Nystatin: antifungal belonging to the polyene group. It is a pale yellow substance in the form of a powder. Like other antifungals, nystatin is of bacterial origin. It was isolated in 1950 by Elizabeth Lee Harren of a bacterium called *Streptomyces Noursei* [5]. Nystatin is a known antifungal from the polyene family. Due to Nystatin limited solubility and high toxicity, it is used mainly to treat oral and dermal fungal infections [6]. It has a therapeutic role for many fungi and yeasts, including *Candida* [7]. It has an effective role in killing and inhibiting the growth of fungistatic and fungicidal by working on degenerative changes in the walls of fungal cells and its association with ergosterol, which is an essential element in the membranes of fungal cells found in genera the *candida specious* which leads to holes in the cell walls and thus leakage of potassium and the exit of the rest of the components from inside the cells to outside the cells, which leads to the death of the germ cell [8].

### 1.1. Neomycin Sulfate

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*, *Enterobacter*. Neomycin was discovered in 1949 by microbiologist Selman Waksman and his student Hubert Lechevalier at Rutgers University. Neomycin received approval for medical use in 1952 [9]. It is produced naturally by the bacterium *Streptomyces fradiae* [10]. Synthesis requires specific nutrient conditions in either stationary or submerged aerobic conditions. The compound is then isolated and purified from the bacterium [11].

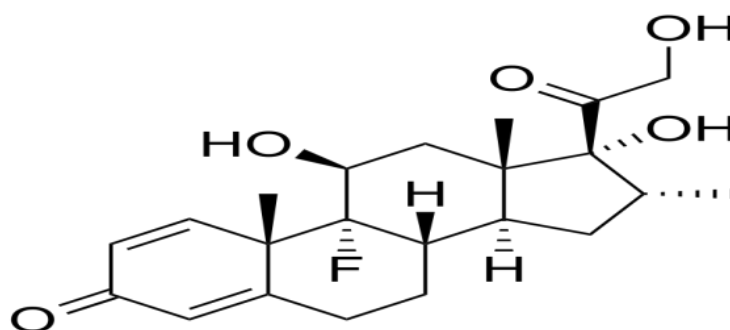
Mechanism of action - Neomycin kills and inhibits the action of the bacterial cell by inhibiting the formation of the bacterial cell wall by preventing the binding of trans Peptidation to Peptoglycol, which is the main component of the bacterial cell wall, thus increasing the activity of enzymes degrading the cell wall. By a process known as autolysis) Hydrolases(ureintolysins) [12].



$$M_w = 615.629 \text{ g/mol} \quad \text{C}_{23}\text{H}_{47}\text{N}_5\text{O}_{18}$$

**Figure (2).** The chemical structure of neomycin sulfate compound.

Dexamethasone: One of the most important steroidal drugs that play an important role as anti-inflammatory and anti-allergic, it is a white crystalline water-soluble powder [Figure (3)]. Dexamethasone was first synthesized in 1957 by Philip Showalter Hench and was approved for medical use in 1958 [13].



$$M_w = 615.629 \text{ g/mol} \quad \text{C}_{23}\text{H}_{35}\text{FO}_6$$

**Figure (3).** The chemical structure of dexamethasone compound.

## 2. Methodology

The examination was carried out in the laboratories of Al-Razi Research Center and the acceptance certificate was obtained by the above center. Other forms were also sent for the purpose of conducting the field assessment. The results were good and the acceptance certificate was obtained by the Veterinary Department of the Veterinary Hospital.

## 3. Experimental Procedure

### 3.1. The Raw materials and devices use:

Raw materials are nystatin, Neomycin sulfate, dexamethasone, lanolin, Vaseline, and additives. Devices used are Magnetic stirrer, 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. Preparing (100) grams of the ointment as follows:

1. Weigh 2.4 g of nystatin, 0.35 g of neomycin sulphate (0.05 g) dexamethasone and put them in a 250 ml dry glass beaker, add 5 ml ethanol and mix well in 30 minutes.
2. Vaseline is added to it after heating it at a temperature of 60°C and added to step 1 with stirring and heating at a temperature of 60°C until the active substance melts (dissolving- miscibility).
3. The rest of the materials are added successively and as shown below.
4. Add the rest of Vaseline to complete (mixing until homogenization) the weight to 100 g.
5. Samples of ointment for biological analysis were sent.
6. Forms were sent for clinical evaluation.

#### 4. Results and Discussion

The results of the microbiological examination showed 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 Ibn Sina Research Center, where its effectiveness was (100%) and it is within the constitutional limits of veterinary pharmacopoeia (90-110%). A stable and stable composition was reached by studying the stability at different temperatures at (25, 35) °C for a period of 3 months (Table 2), where it was noted that the effectiveness of the preparation is not affected much over time, because the effectiveness of nystatin remained within the permissible limits and the decrease in effectiveness was very limited. This indicates the stability and effectiveness of the drug combination. The field examination also showed its therapeutic efficacy for cases of fungal diseases and skin infections in cats. The opposition obtained a certificate of acceptance send from the veterinary department / veterinary hospital.

##### 4.1. Stability study

The stability of the product was monitored at room temperature for a period of (3) months, according to the results listed below. Initial evaluation (time zero) 100% according to the microbiological examination [14].

**Table (1).** Specification of raw material in formula.

No.	Substance	Reference	Description	Solubility
1	Nystatin	B.P2007 (6)	Yellowish powder	Slightly soluble in water, freely soluble in acetone
2	Neomycin sulfate	B.P 2007 (6) Martindale 34,27,25(4)	White or slightly yellow powder, hygroscopic.	soluble in water
3	Dexamethasone	USP 2008	White, crystals	soluble in water
4	Vaseline	B.P2013	Odorless and tasteless	Soluble in water, alcohol, ether, chloroform

**Table (2).** Stability study at temperatures (25, 35) °C.

No.	Follow	activity of nystatin, neomycin, and dexamethasone	
		25°C	35°C
1	Follow after 1 month	100%	100%
2	Follow after 2 month	100%	100%
3	Follow after 3 month	100%	100%

**Table (3).** Concentration of Nystatin, neomycin sulfate and dexamethasone zero time.

No.	Subject	Concentration (%)
1	Nystatin	100
2	Neomycin sulfate	100
3	Dexamethasone	100

## 5. 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) in cases of bacterial infections of the outer and middle ear, as it gave fruitful results in the work.

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