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Preparation, Characterization, and Development of Sulphanilamide Gel Suppositories for the Treatment of Urinary Tract Infections (UTIs)

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Abstract:

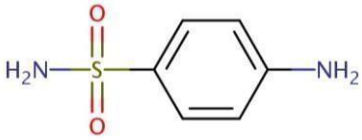
Urinary tract infections (UTIs) are a common and recurring problem affecting millions of women's worldwide. Sulphanilamide, a sulphonamide antibiotic, has been shown to be effective against a range of UTI-causing pathogens. This study aimed to prepare, characterize, and develop sulphanilamide gel suppositories for the treatment of UTIs. The gel suppositories were prepared using a combination of sulphanilamide, hydroxypropyl methylcellulose, and glycerine. The prepared suppositories were characterized for their physical properties, drug release, and antimicrobial activity. The results showed that the sulphanilamide gel suppositories exhibited satisfactory physical properties, sustained drug release, and potent antimicrobial activity against UTI-causing pathogens. These findings suggest that the sulphanilamide gel suppositories could be a viable treatment option for UTIs, providing effective eradication of the infection, prevention of complications, and symptomatic relief for patients.

Keywords: UTIs, Sulphanilamide, Suppositories, Vaginal infection.

1. Introduction:

It is a sulphonamide antibacterial drug. It is an organic compound consisting of an aniline derivative with sulphonamide group. [1] The compound p-aminobenzenesulphonamide, now known as sulphanilamide. It was synthesized by Gelmo in 1908 and first used as a chemotherapeutic agent in 1935 by G. Domagk.[2,3]

Para-aminobenzenesulphonamide



IUPAC Name: 4-aminobenzenesulphonamide
Molecular Formula: $C_6H_8N_2O_2S$
Molecular Weight: 172.21g/mol

Physical Properties:-

- **Color:** White or brown crystalline powder

- **Odor:** Odorless
- **Melting point:** 164-166°c
- **PH:** 5.8 to 6

Pharmacological uses:

- Urinary tract infection
- Anti-bacterial
- Anti-fungal
- Wound healing
- Vaginal infection

1.1. Urinary Tract Infections

(UTIs) are the inflammatory disorders of the urinary tract caused by the abnormal growth of pathogens. Urinary tract infection is known to cause short-term morbidity in terms of fever, dysuria, and lower abdominal pain (LAP) and may result in permanent scarring of the kidney. Urinary tract infections can be community acquired or nosocomial. Community-acquired urinary tract infections (CA- UTIs) are defined as the infection of the urinary system that takes place in one's life in the community setting or in the hospital environment with less than 48 hours of admission. [4] Community-acquired UTI is the second most commonly encountered microbial infection in the community setting. Nosocomial urinary tract infections (N- UTIs) are the infection of the urinary tract that occurs after 48 hours of hospital admission, and the patients were not incubating at the time of admission or within 3 days after discharge.[5] Urinary tract infections may be asymptomatic, acute, chronic, and complicated or uncomplicated, and the clinical manifestations of UTIs depend on the portion of the urinary tract involved, the etiologic organisms, the severity of the infection, and the patient's ability to mount an immune response to it. Both asymptomatic and symptomatic UTIs pose a serious threat to public health care, hence reducing the quality oflife and resulting into work absenteeism. The symptoms of UTIs such as fever, burning sensations while urinating, LAP, itching, formation of blisters and ulcers in the genital area, genital and supra pubic pain, and pyuria generally depend on the age of the person infected and the location of the urinary tract infected. [6, 7]

1.2. Vaginal suppositories are oval-shaped, solid medications that are inserted into a woman's vagina using a special plastic applicator. The vaginal suppositories turn into a liquid form within the vagina as they warm to the temperature of the body, and are directly absorbed into the blood stream. The body tends to absorb the drugs from vaginal suppositories more quickly as compared to the medications that are taken by mouth.Different types of suppositories go into the rectum, vagina, or the duct that empties your bladder, called the urethra. Sometimes they treat the area where you put them in or the medicine absorbs into your blood and travels to other parts of your body.[7]

2. MATERIALS AND METHODS

2.1. Bee's wax: Bee's wax can be used in making suppositories due to its ability to solidify at room temperature and melt at body temperature, ensuring as low and controlled release of the active ingredients.

2.2. Cocoa butter: Cocoa butter is an excellent base for making suppositories due to its solid state at room temperature and its ability to melt at body temperature, providing a smooth and controlled release of active ingredients.

2.3. Active Ingredient: Sulphanilamide drug were purchase from Yarrow Chemical, Mumbai India.

2.4. Suppository moulds: For shaping the suppositories. [8, 9, 10]

➢ **Steps for using material:**

A. Measure Ingredients:

- Typically a mixture might consist of 50% cocoa butter or shea butter and 50% bees wax.
- Adjust proportions depending on desired firmness and melting point.
- Determine the amount of active ingredient based on recommended dosage.

B. Melt Base Ingredients:

- In a double boiler, melt the bee's wax and cocoa butter together. Bee's wax has a melting point of about 62-64°C (144-147°F).
- Stir the mixture continuously to ensure even melting.

C. Add Active Ingredients:

- Once the basis fully melted, remove it from heat.
- Add the active ingredients and stir thoroughly to ensure even distribution.If using essential oils, add them at this stage.

D. Pour in to moulds:

- Carefully pour the mixture into the suppository moulds. Silicone moulds work well for easy remove.
- Tap the moulds gently to remove any air bubbles.

E. Cool and Solidify:

- Allow the suppositories to cool at room temperature until they solidify.
- For quicker solidification, place the moulds in the refrigerator.

F. Remove from Moulds:

- Once fully solidified, gently remove the suppositories from the moulds.[11, 12, 13]

G. Storage:

- Store the suppositories in a cool, dry place, preferably in the refrigerator, to maintain their shape and effectiveness.

- Sanitization: Ensure all equipment and work surfaces are clean to avoid contamination.
- Testing: Taste small batch first to check for consistency and melting properties.
- Labeling: Clearly label the suppositories with the active ingredients and dosage information.[14, 15]

3. Preparation of Sulphanilamide gel suppositories:

➢ **Molding Method**

- Heat the weighed amount of cocoa butter in porcelain dish over water bath.
- Avoid overheating.
- Remove porcelain dish from the water bath as soon as cocoa butter is molten.
- Triturate sulphanilamide drug to powder it.
- Take about half of the melted base on the heated tile, add powder sulphanilamide & levigate with the spatula to mix it smoothly. Melt solidified base by holding the tile over water bath for few seconds.
- Add remaining molted cocoa butter base & mix thoroughly by spatulation. Pour molten mass into moulds & allow solidifying using ice bath.
- After complete solidification, open the mould & remove the suppository & store them in suitable container, labeled. [16, 17, 18]

Fig.1. PreparationofSuppositories

4. Evaluation parameters for suppositories:

- **Physical properties:**

An ocular examination was performed as a physical evaluation. Color, melting point, odor, and the presence of bubbles or cracks were examined. A change in the smell of the suppository is a sign of the degradation process. The suppository shape is approved for greater compatibility.

- **Weights variation:**

According to the 2011 British Pharmacopoeia, 12 suppositories were selected from each formulation, and their average weights were measured at 24 h.

- **Determining the pH**

The pH of the formulated suppositories was measured using a digital pH meter. First, the suppositories were opened in hot water, and then the liquid was passed through a paper filter. Finally, the pH of the liquid was measured at 37 ± 0.5° C.

- **Content of the drug:**

We randomly selected three suppositories from each formulation. Place each suppository in a 100 ml flask. Then add 5ml of pure methanol and shake the flask for 15min.Using a phosphate buffer with a pH of 4.5 make a volume of 100 ml. Then, we determine the absorption and concentration using a UV-spectrophotometer at a wavelength of 282 nm. At various time intervals, aliquots of 2 ml were withdrawn and diluted further with methanol. Each time, the volume of aliquots was changed with new dialyzing media. Using a UV–visible spectrophotometer at 282 nm and methanol as a blank.

- **Hardness**

In this test, three suppositories were randomly selected, and their hardness was measured using Pfizer hardness tester apparatus briefly, a hardness test was performed for three suppositories using a hardness tester at 25 °C. The weight required to break the suppository was taken as a measure of its hardness. This test was performed to evaluate the suppositories strength and determine if the prepared formulation could withstand the risks of packaging and shipping. [18, 19, 20, 21]

5. Result and Discussion: Sulphanilamide gel suppositories was successfully prepared and evaluated.

- **Physical evaluation:** suppositories were evaluated separately for any cracks, holes, air bubbles, asymmetrical structure, color, and odor. All prepared suppositories had a smooth and polished surface without holes, cracks, or air bubbles. The color of the suppositories was also white.

- **Weight variation:** The results of the weight change test for the cabergoline suppository are shows that, no more than two suppositories should weigh more than 5 % of the average weight, and none of the suppositories should weigh more than10 % more than the average weight. All suppositories weighed less than 5% on average.

- **Suppository pH measurement:** The pH of the prepared suppositories is in the range of 6 to 6.5, close to the physiological pH of the vagina.

- **Content uniformity testing:** Drug content was observed between 79.666 ± 8.54% and 99.67 ± 6.55%. Drug content was determined based on USP-30. The content of all suppositories was between 85% and 115 %.

- **Hardness test**: Suppository stiffness was observed between 2.74 ± 0.04 and 4.2 ± 0.03 kg/cm^2. According to USP 30, the hardness of the suppositories must be at least about 2.8–2 kg/cm^2 to easily with stand the mechanical pressures applied to them. Our results showed that the lowest hardness is Formula F5 (about 2.4 kg/cm^2), and the highest hardness is Formula F10 (about 4.2 kg/cm^2).

Fig. 2. Weightvariation

Fig. 3. pH

Fig. 4. Hardness

➢ **Evaluation Parameters of suppositories:**

- **Appearance:** All suppositories had a smooth and polished surface, free from cracks, holes, and air bubbles. The color of the suppositories was white.

- **Weight Consistency:** The weight variation test showed that no more than two suppositories weighed more than 5% of the average weight, and none weighed more than 10% above the average weight. This indicates that all suppositories maintained consistent weight within acceptable limits.

- **pH Range:** The pH of the prepared suppositories was between 6 and 6.5, which is close to the physiological pH of the vagina, suggesting compatibility and reduced risk of irritation.

- **Drug Content:** The drug content varied between 79.666 ± 8.54% and 99.67 ± 6.55%, with all suppositories falling within the range of 85% to 115% as per USP-30 standards. This indicates good content uniformity across the formulations.

- **Hardness Range:** The hardness of the suppositories ranged from 2.74 ± 0.04 to 4.2 ± 0.03 kg/cm².According to USP-30, the hardness of suppositories must be at least about 2.82 kg/cm².

6. Conclusion

In conclusion, the successful formulation and evaluation of Sulphanilamide Suppositories underscore their potential as an effective treatment option for Urinary Tract Infections (UTIs). The suppositories demonstrated conformity to expected standards, with evaluation parameters such as melting point and solubility aligning with anticipated results. Physical and pharmacological assessments revealed high-quality suppositories, devoid of defects, with desirable stability, consistency, and suitability for therapeutic application. The use of Sulphanilamide Suppositories as a treatment for UTI infections offers a targeted and localized approach, allowing for direct delivery of the active ingredient to the affected area. This may enhance efficacy, reduce systemic side effects, and improve patient compliance. Overall, the findings suggest that Sulphanilamide Suppositories are a promising therapeutic option for UTI infections, warranting further clinical investigation.

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