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FORMULATION AND EVALUATION OF LACTIC ACID SUPPOSITORIES

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Abstract:

The vaginal microbiota in bacterial vaginosis (BV) typically has low abundance of lactic acid producing lactobacilli. Lactic acid has properties that may make it effective for treating BV and/or restoring an optimal lactobacillus-dominated vaginal microbiota. We conducted a systematic review to describe the effect of intravaginal lactic acid-containing products on BV cure, and their impact on vaginal microbiota composition. The optimal vaginal microbiota of reproductive aged women is typically characterized by dominance of lactic acid producing Lactobacillus species including Lactobacillus crispatus, Lactobacillus gasseri and Lactobacillus jensenii Lactic acid containing products have been evaluated for BV treatment in clinical trials, and several over-the counter lactic acid-containing products are marketed to treat BV or support optimal vaginal microbiota. However, the use of these products is not recommended by any treatment guidelines.

We conducted a systematic review with two objectives: 1) to describe the effect of intravaginal lactic acid-containing products for BV cure (assessed using an established diagnostic method), and 2) to describe the impact of intravaginal lactic acid-containing products on the vaginal microbiota (assessed using molecular methods). Studies were eligible if they were randomized controlled trials (RCT) where an intravaginal lactic acid-containing product was assessed in comparison to either no treatment, a placebo or a recommended antibiotic treatment for BV. No restrictions were placed on number of participants enrolled. Studies of pregnant women and post-menopausal women were excluded.

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REVIEW OF LITERATURE:

The role of Lactobacillus probiotics in the treatment or prevention of urogenital infections: a systematic review

- The review found a significant benefit for treatment of recurrent bacterial vaginosis with certain *Lactobacillus* strains, but evidence in the prevention or treatment of urinary tract infection and or vulvovaginal or vaginal candidiasis was uncertain. Potential limitations in the review process and uncertainties about the quality of included studies make the reliability of the authors' conclusions unclear

- All clinical controlled trials that evaluated use of *Lactobacillus*-containing probiotics compared with no treatment or a comparator in treatment or prevention of bacterial vaginosis, vulvovaginal candidiasis or urinary tract infection in adults were eligible for inclusion. Studies that focused on colonization or restoration of normal vaginal flora were eligible. Studies were excluded if data were not provided to calculate relative risk.

- Most studies used intravaginal preparations of Lactobacilli, mostly pessaries or suppositories but also douches and tampons. One study used both oral and vaginal lactobacilli.

- The remaining studies used oral preparations (one used yogurt). Doses were no less than $1x10^6$ CFU lactobacilli. Dosing frequency varied from once to twice daily to once weekly.

- Treatment duration ranged from four days to 19 months. Lactobacilli strains used included: *L. acidophilus, L. rhamnosus* (GG and GR-1), *L. fermentum* RC-14 (renamed *L.reuteri), L. delbrueckii, L. crispatus* and *L. gasseri* alone or in combination. (Further details of interventions were reported.) Definitions of criteria used for diagnosis of the three infections were provided.

- Bacterial vaginosis was evaluated using Amsel's criteria and/or Nugent's score. Normal vagina flora was evaluated using Nugent's score or modified Normal Flora Index (details were reported). Most studies were of women in an outpatient setting. Most participants were healthy premenopausal non-pregnant women. In a minority of the studies the women receive concomitant antibiotics.

Assessment of study quality

Methodological quality was assessed by two authors independently in terms of blinding, randomisation, follow-up time, loss to follow-up and use of a placebo.

Data extraction

The number of events for each outcome was extracted in order to calculate relative risk (RR) and 95% confidence intervals (CI). Two reviewers extracted data independently.

METHODS OF SYNTHESIS:

A narrative synthesis was performed as the studies were heterogeneous. Results were summarised in a tabular form.

Results of the review

Twenty-five relevant studies were identified (n=2,348): 17 randomized controlled trials (RCTs) (n=1,993), which comprised nine double-blind, one single-blind and nine placebo-controlled; and eight before-after studies with historical controls (n=355), which comprised one double-blind and placebo-controlled studies. Of two studies each of prevention and treatment of vulvovaginal candidiasis, only one prospective cross-over trial found a significant benefit for prevention (RR 0.39, 95% CI 0.17 to 0.70). One RCT of the five studies of prevention of urinary tract infections found a significant benefit with both lactobacilli (RR 0.42, 95% CI 0.22 to 0.67) and lactobacilli growth factor (RR 0.63). There were nine studies of treatment of bacterial vaginosis. Of these, five RCTs and one quasi-experimental trial showed a significant reduction in infection (RR range 0.03 to 0.43). Data for adverse events were reported for seven studies: four reported no side effects; one reported headaches and increased appetite; and two reported itching or burning sensations. Four RCTs (of seven studies) of *Lactobacillus* colonization or restoration of normal vaginal flora found a significant positive benefit. Use of certain *Lactobacillus* strains such as *L. rhamnosus* GR-1 and *L. reuteri* for prevention and treatment of recurrent urogenital infection had promise, especially for recurrent bacterial vaginosis. Scant data on use of probiotics for urinary tract infection and vulvovaginal candidiasis precluded definitive recommendations.

- Probiotics are increasingly being used to treat and prevent urogenital infections. However, a critical assessment of their efficacy in major urogenital infections is lacking. We report the results of a systematic review to determine the efficacy of probiotics for prevention or treatment

of three major urogenital infections: bacterial vaginosis, vulvovaginal candidiasis, and urinary tract infection.

- Using multiple computerize ed databases, we extracted data from clinical trials using a lactobacillus-containing preparation to either prevent or treat a urogenital infection. Of 25 included studies, 18 studies used lactobacillus preparations for treatment or prevention of urogenital infections and seven studies focused solely on vaginal colonization
- Four studies included patients with vaginal candidiasis, five included patients with urinary tract infections, and eight included patients with bacterial vaginosis. One included several types of genitourinary infections.

- Overall, lactobacilli were beneficial for the treatment of patients with bacterial vaginosis. No clear benefit was seen for candidiasis or urinary tract infection. Studies were heterogenous, with some limited by a small population size.

- In conclusion, the use of certain lactobacillus strains such as *L. rhamnosus* GR-1 and *L. reuteri* for prevention and treatment of recurrent urogenital infection is promising, especially for recurrent bacterial vaginosis.

- Scant data on the use of probiotics for urinary tract infection and vulvovaginal candidiasis precludes definitive recommendations. Further research and larger studies on types of lactobacilli strains, dosage of lactobacilli, optimal route and vehicle of administration are needed.

Quick Points

Probiotic lactobacilli are commonly used choices for treating and preventing urogynecologic infections.

- Although clinical practice recommendations were limited by the strength of evidence, probiotic interventions appear to be effective in treatment and prevention of urogenital infections as an alternative or co-treatment.

- None of the probiotic interventions were associated with serious adverse events.

- More well-designed clinical research studies are needed on probiotics used to treat or prevent urogenital infections in women.

- If used as co-treatments, other evidence suggests that antibiotic and probiotic interventions should be separated by at least 2 to 4 hours to avoid the destruction of the live microorganisms in the gastrointestinal tract

- There is a clear link between vaginal microflora and urogenital infections. Independent of personal hygiene, the large varieties of microbes that populate the vagina originate from the gastrointestinal tract. Healthy vaginal microflora is characterized by a dominance of Lactobacillus bacterial species.A number of scientific investigations have demonstrated that the gastrointestinal and vaginal microflora can be modified with probiotic supplementation to treat and prevent genitourinary infections. Probiotics are live bacteria that confer a health effect on the host when they are administered in sufficient amounts. Therefore, probiotics used to prevent and treat genitourinary infections contain Lactobacillus species, since the target is the vaginal microflora. The mechanisms of action of probiotics include acidification of the mucosal surface, prevention of the adherence of pathogens, the production of substances such as vitamins and immune modulators, and synergistic action with the host immune system. Some species of Lactobacillus produce hydrogen peroxide, which further acidifies the vaginal mucosa. This property makes Lactobacillus a common probiotic choice for treating and preventing urogynecologic infections.

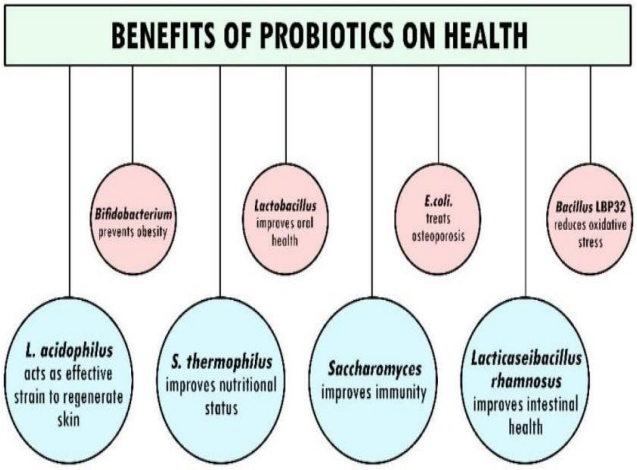


Fig. 1

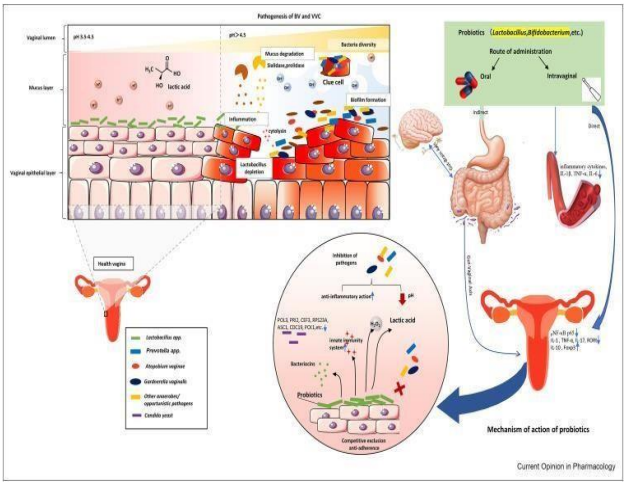


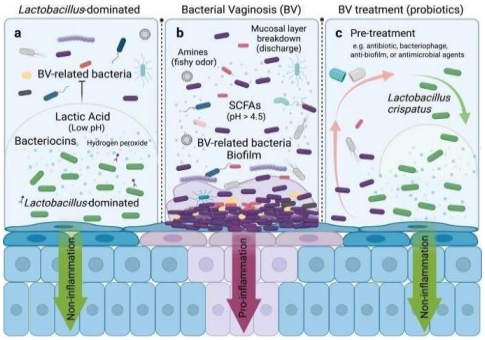
Fig. 2

OVERVIEW OF THE STRATEGY ON VAGINOGSIS TREATMENT WITH PROBIOTICS

a) Lactobacillus-dominated vaginal microbiome environment. Vaginal Lactobacillus species, such as Lactobacillus crispatus, produce lactic acid, bacteriocins, and hydrogen peroxide (H_2O_2), which may provide protection against bacterial vaginosis (BV) related bacteria and other infections.

b) BV microbiome environment. BV-related bacteria (mainly Gardnerella) induce inflammation in the vaginal tract and form a biofilm on vaginal epithelial cells. The latter probably increases antibiotic resistance and refractoriness to probiotic treatment. Short chain fatty acids (SCFAs) produced by BV-related bacteria, increase vaginal pH. In addition, catabolism of amino acids and mucosal proteins results in amines and a thinner mucosal layer in the vaginal tract.

c) Treatment of BV with probiotics. Pretreatment such as antibiotic, bacteriophage, antibiofilm, or antimicrobial agents, in combination with vaginal probiotic species and vaginal administration, increase the probability of successful colonization. Note: figure was created with BioRender.com.



The standard of care treatment for BV is antibiotics. Live biopharmaceutical products, defined by the United States Food and Drug Administration (FDA) and the European Pharmacopeia as “a biological product that contains live organisms; is applicable to the prevention, treatment, or cure of a disease or condition of human beings; and is not a vaccine”, or generally called “probiotics,” defined as “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host” by the Food and Agriculture Organization of the United Nations and the World Health Organization and revised by the International Scientific Association for Probiotics and Prebiotics, have been evaluated as BV treatments in clinical trials for decades with mixed results.

Recently, vaginal microbiome transplantation (VMT), the process of transferring the microbiome of a healthy donor to an individual as a therapeutic alternative, has been tested to restore the vaginal microbiome. In this

review, we discuss the advantages and disadvantages of these interventions and provide our considerations of what needs to be contemplated for future clinical trials with probiotics.

INTRODUCTION:

Definition of Suppositories:

A suppository is a dosage form used to deliver medications by insertion into a body orifice where it dissolves or melts to exert local or systemic effects. There are three types of suppositories, each to insert into a different sections: rectal suppositories into the rectum, vaginal suppositories into the vagina, and urethral suppositories into the urethra of a male.Suppositories are ideal for infants, elderly individuals and post-operative patients, who are unable to swallow oral medications, and for individuals experiencing severe nausea and/or vomiting.

Composition:

Several different ingredients can be used to form the base of a suppository: cocoa butter or a similar substitute, polyethylene glycol, hydrogels, and glycerinated gelatin. The type of material used depends on the type of suppository, the type of drug, and the conditions in which the suppository will be stored.

Rectal suppositories:

In 1991, a study on suppository insertion in *The Lancet* found that the "torpedo" shape helps the device to travel internally, increasing its efficacy. The findings of this single study have been challenged as there is insufficient evidence on which to base clinical practice. Rectal suppositories are intended for localized or systemic action to relieve pain, constipation, irritation, inflammation, nausea and vomiting, fever, migraines, allergies, and sedation.

Fig 4

Glycerin suppositories (laxative)

Vaginal eubiosis and dysbiosis:

The vagina and ectocervix, comprising the lower female reproductive tract (FRT), are composed of a rarely keratinized stratified squamous epithelium, resting on a lamina propria, that is bathed in mucous and colonized with microbiota that can have commensal (benefit of one of the organisms, without effect for the other), mutualistic (both organisms' benefit) or parasitic (microbes profit at the expense of the host) roles. The vaginal microbiota, during eubiosis in reproductive-age women, is typically dominated by the distinct *Lactobacillus* spp., *Lactobacillus crispatus*, *Lactobacillus gasseri*, *Lactobacillus iners* and *Lactobacillus jensenii*, respectively, most of which produce large amounts of lactic acid. In contrast, vaginal dysbiosis is characterized by the presence of polymicrobial populations with either a modest lactobacillus load (intermediate microbiota) or no lactobacilli (bacterial vaginosis, BV). BV is a very common yet poorly understood condition in reproductive-age women that is associated with adverse sexual and reproductive health outcomes.

Vaginal eubiosis is characterized by the presence of beneficial lactic-acid producing microbiota predominantly fromt hegenus *Lactobacillus*. *Lactobacillus* spp., naturally or administered as probiotics, may establish vaginal eubiosis by killing dysbiotic microbes, and many types of pathogens, with acidic lactic acid. They may also release other antimicrobial factors such as bacteriocins . While many lactobacillus-based probiotics have been selected on the basis of hydrogen peroxide (H_2O_2) production, recent studies demonstrate that lactic acid is a major antimicrobial factor produced by lactobacilli. This review focuses on the antimicrobial, antiviral and immunomodulatory properties of lactic acid, the major organic acid metabolite produced by lactobacilli. The differential effects reported for lactic acid isomers and their protonated forms will be discussed, as well as how lactobacilli generate lactic acid, by using amylase breakdown products of glycogen, We also review clinical studies that have evaluated the use of lactic acid or lactobacilli probiotics in preventing or treating bacterial vaginosis, and studies that are providing a clearer understanding of the properties of lactic acid production by *Lactobacillus* spp. which could lead to the development of improved vaginal probiotics.

The vaginal microbiomes harbored by women can differ based on cultural, behavioral and genetic

factors. Caucasian women are predominantly colonised with *L. crispatus* microbiomes, while African and Hispanic women tend to be colonised with *L. iners* or polymicrobial microbiomes.

The vaginal microbial communities differ in their stability in the face of intrinsic (e.g. sex hormones, menses) and extrinsic (e.g. sexual intercourse, vaginal hygiene practices) disturbances. *L. crispatus* dominated microbiomes are relatively stable. while most, but not all, strains of *L. iners* appear to be less effective at preventing episodes of bacterial dysbiosis

HISTORY

Suppositories, pessaries and bougies have been prescribed for the last 2000 years but their popularity as a medicinal form increased from around 1840 - suppositories for constipation, haemorrhoids and later as an alternative method of drug administration, pessaries for vaginal infections and bougies for infections of the urethra, prostate, bladder or nose.

MANUFACTURE

The basic method of manufacture was the same for each preparation, the shape differed. Suppositories were "bullet" or "torpedo" shaped, pessaries "bullet"

2. COMPRESSION MOULDING

Compression molding is a method of preparing suppositories from a mixed mass of grated suppository base and medicaments which is forced into a special compression mold using suppository making machines. The suppository base and the other ingredients are combined by thorough mixing. The base softens because of the friction in the process. A mortar and pestle can be used on small scale. On the other hand, large-scale manufacturing involves mechanically operated kneading mixers and a warmed mixing vessel. In the compression machine, the suppository mass is placed into a cylinder which is then closed. After that from one end pressure is applied to release the mass from the other end into the suppository mold or die. When the die is filled with the

shaped but larger and bougies long and thin, tapering slightly.A base was required that would melt at body temperature. Various oils and fats have been utilised but, until the advent of modern manufactured waxes, the substances of choice were theobroma oil (cocoa butter) and a glycerin-gelatin mixture.labelled with the doctor's instructions**.**

1.HAND ROLLING

It is the simplest and oldest method of suppository preparation and may be used when only a few suppositories are to be prepared in a cocoa butter base. It has the advantage of avoiding the necessity of heating the cocoa butter.

By triturating grated cocoa butter and active ingredients in a mortar, a plastic-like mass is prepared. The mass is formed into a ball in the palm of the hands, then rolled into a uniform cylinder with a large spatula or small flat board on a pill tile. The cylinder is then cut into the appropriate number of pieces which are rolled on one end to produce a conical shape.The suppository “pipe” or cylinder tends to crack or hollow in the center, especially when the mass is insufficiently kneaded and softened.

mass, a movable end plate at the back of the die is removed and when additional pressure is applied to the mass in the cylinder, the formed suppositories are ejected. The endplate is returned, and the process is repeated until all of the suppository mass has been used. When active ingredients are added, it is necessary to omit a portion of the suppository base, based on the density factors of the active ingredients.

3. FUSION MOULDING

Fusion Moulding process involves the following steps:

- First melting the suppository base.
- Then the drug is either dispersed or dissolved in the melted base.
- The mixture is then removed from the heat and poured into a suppository mold.
- The melt is allowed to congeal
- Now the suppositories are removed from the mould.

4. SUPPOSITORIES MOULDING

Small scale moulds are capable of producing 6 or 12 suppositories in a single operation. Industrial moulds produce thousands of suppositories per hour from a single moulding.

5. CALIBRATION OF MOULDING

The calibration of mold is necessary because the size of the suppositories remains the same from a particular

mold but their weight varies because the density of the different types of bases and the medicaments used are different. The first step is to prepare molded suppositories from base material alone. The suppositories are combined and the average weight is recorded. To determine the volume of the mold, the suppositories are melted in a calibrated beaker, and the volume of the melt is determined.

6. LUBRICANTS USED IN MOULDS

Cocoa butter and glycerol-gelatine bases are required lubrication of molds. This prevents the stacking of bases to the wall of the mold cavity. It is also useful in the easy removal of suppositories from the molds. The lubricants form a film between the wall of the mold cavity and the base of suppositories
so, they prevent adhering of bases to the molds. The nature of lubricants should be different from the nature of bases.

Lubricant must be compatible with medicament or adjuncts. In industry, silicone fluid is used as a lubricant. Mould is lubricated using a pad of gauze or muslin or with a small fairly stiff brush. Cotton wool is not used because some fibres adhere to the mould. Excess lubricant can be removed by inverting the mold on a clean white tile.

EXAMPLES:

A.For cocoa butter bases

1) Alcohol (90%) – 50 ml
2) Glycerol – 10 ml
3) Softsoap 10 gm

B.For the glycerol-gelatin base

1) Liquid paraffin or Arachis oil is used as a lubricant

PACKAGEING:

Suppositories must be packed in such a manner that they do not touch each other.

Poorly wrapped and packaged suppositories can lead to staining, breaking, or deformation by melting caused by the adhesion. Suppositories usually are foiled in tin or aluminum, paper, or plastic strips. Overwrapping is done by hand or machine.

Hand-packing yields a non-uniform product so machines are utilized to overcome this problem and machines can wrap 8000 suppositories per hour.

STORAGE:

Suppositories should be protected from heat, preferably by storing in the refrigerator.

Polyethylene glycol suppositories and suppositories enclosed in a solid shell are less prone to distortion to a temperature slightly above body tempt.

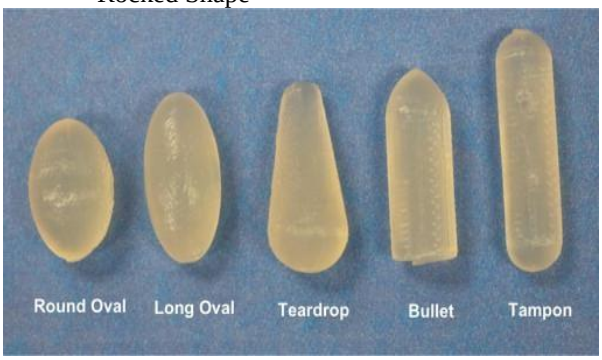
LABELLING:

Suppositories should be labelled as:

- "STORE IN A COOL PLACE"
- "FOR EXTERNAL USE ONLY"
- "NOT TO BE TAKEN OORALL

Different shapes and sizes of suppositories designed in CURA, Solidworks in combination with Ultimaker

- Torpedo-shaped
- bullet-shaped
- Rocked Shape



Suppositories as a dosage form

ADVANTAGES:

- Can exert local effect on rectal mucosa.
- Used to promote evacuation of bowel.
- Avoid any gastrointestinal irritation.
- Can be used in unconscious patients.
- Can be used for systemic absorption of drugs and avoid first-pass metabolism.

Suppositories as a dosage form

DISADVANTAGES:

- The problem of patient acceptability.
- Suppositories are not suitable for patients suffering from diarrhea.
- not suitable for drugs that irritate rectal mucosa.
- Incomplete absorption may be obtained because suppository usually
- promotes evacuation of the bowel.

Mode of insertion of suppositories

- Remove suppository from its package.
- Insert small tapered end first with index finger for the full length of the finger.

- May need to be lubricated with a water-soluble gel to ease insertion.
- The use of an examination glove or a finger cot can ease insertion by protecting the rectal wall from fingernail.

Vaginal suppositories

- Pessaries are a type of suppository intended for vaginal use.
- They have various shapes, usually ovoid, with a volume and consistency suitable for insertion into the vagina.
- Vaginal suppositories are commonly used to treat gynecological ailments, including vaginal infections such as candidiasis.

Application should follow a specific technique:

- Begin with an empty bladder and washed hands.
- Open the container and place dose in applicator.
- Lubricate applicator with water-soluble lubricant if not pre-lubricated.
- Lie down, spread the legs, open the labia with one hand, and insert the applicator about two inches into the vagina with the other hand.
- Release labia; use free hand to push applicator plunger.
- Withdraw the applicator and wash the hands.

Urethral suppositories

The urethral route of administration is application of drug by insertion into the urethra

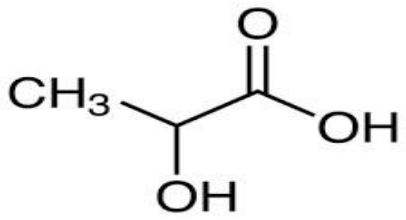
- Urethral delivery may be used to treat
- Incontinence
- Impotence in men Disadvantages
- Inconvenience
- Localized pain

Suppository Base

- Suppositories are drug delivery system where the drugs are incorporated
- into inert vehicle called suppository base.
- The USP lists the following suppository base:
- Cocoa butter
- Cocoa butter substitutes such as vegetable oils modified by • esterification, hydrogenation,.
- Glycerinated gelatin
- Mixtures of PEGs of various molecular weights.

Experimental work

Drug Profile: Lactic acid



Structure of lactic acid

Introduction: Lactic Acid, DL- is the racemic isomer of lactic acid, the biologically active isoform in humans. Lactic acid or lactate is produced during fermentation from pyruvate by lactate dehydrogenase. This reaction, in addition to producing lactic acid, also produces nicotinamide adenine dinucleotide (NAD) that is then used in glycolysis to produce energy source adenosine triphosphate (ATP).

Lactic acid appears as a colorless to yellow odorless syrupy liquid. Corrosive to metals and tissue.

Formula: $C_3H_6O_3$

Molar mass: 90.08 g/mol

IUPAC Name: 2-Hydroxypropanoic acid

Melting point: 16.8 °C Boiling point: 122 °C

Classification: Alpha hydroxy acid, Organic acid

Uses:

1) use to make dairy product.
2) As a food's preservative.
3) Used to treat bacterial vaginosis. (BV)

Why do we use the Lactic acid in bacterial vaginosis?

The optimal vaginal microbiota of reproductive aged women is typically characterised by dominance of lactic acid producing Lactobacillus species including Lactobacillus crispatus, Lactobacillus gasseri and Lactobacillus jensenii. Women with BV have reduced abundance of these lactobacilli and increased prevalence and abundance of anaerobic and facultative-anaerobic bacteria. *In vitro* studies have shown that lactic acid inactivates BV-associated bacteria and pathogens including Chlamydia

trachomatis, Neisseria gonorrhoeae and HIV via mechanisms independent of acidity alone Lactic acid has also been shown to modulate cervicovaginal epithelial cell functions to prevent C. trachomatis infection.

Lactic acid also has immunomodulatory effects, and can elicit an anti-inflammatory response and reduce production of inflammatory cytokines and chemokines from cervicovaginal epithelial cells in vitro.

Formulation of lactic acid suppositories:

List of material

Sr. No.	Materials
1	Gelatin
2	Glycerin
3	Lactic acid
4	Water

Table 1

List of equiqment

Sr. No.	Equipment
1	Suppositories mould
2	China dish
3	Water bath
4	Tripod stand
5	Stirrer

Table 2

Formula for preparing lactic acid suppositories

Rx

S.R.	Ingredients	Quantity taken
1	Lactic acid	1.5gm
2	Glycerin	21.5ml
3	Gelatin	4.30gm
4	Water	4.9 ml

Table. 3

Above formula is for the preparation of 20 suppositories weighing (1.28 gm. Each) And is calculated as:

A) Quantity of glycerogelatin base required = No. of suppository to be prepared x

Suppository mould weight x correction factor =20 x 1.28 gm. X 1.2 = 30.72 gm.

Now in glycerogelatin base we have to take 14% gelatin and 70 glycerin and 16% water

1. Quantity of gelatin = 30.72 x 14/100 =4.30gm.
2. Quantity of glycerin = 30.72 x 70/100 = 21.5 ml
3. Quantity of the water = 30.72 x 16/100 =4.91 ml

Lactic acid (API): As formulation contain 5% of lactic acid hence, 1. Quantity of lactic acid =30.72 x 5/100 = 1.536.

B) Calculation of the displacement value:

1. Weight of 6 unmedicated suppositories =6 x 1.20gm =7.2gm. (a)
2. Weight of the 6 medicated suppositories =7.18 gm. (b)

3. Weight of the base in the suppositories =95/100 x 7.18 = 6.821gm. (c)
4. Weight of the drug in the suppositories = 5/100 x 7.18 = 0.35 gm. (d)
5. Weight of the base displaced by the drug = 7.2 – 6.8212 = 0.379 gm. (a – c)
6. Displacement value Dv = d/ a-c = 0.35/0.379 =0.92 (Approximately equal to 1)
7. It is also true that the displacement value for the liquid is 1(as our drug is in liquid form) hence we can say that all calculation are correct.

Procedure:

1. The Suppository mould is lubricated with the help of the liquid paraffin and then it is placed in the refrigerator.
2. Weigh the china dish and note it as W1 and W2. (w1=113.08gm, w2=126.4gm)
3. In the china dish W1 take water and gelatin and soaked the gelatin for few minutes.
4. In the china dish W2 take required amount of the glycerin and lactic acid.
5. Take the china dish W2 and heat the content in it for 20 minutes along with constant stirring and place it on the hot water bath and on the other hand heat the china dish containing the soaked gelatin until it liquefy.
6. After gelatin takes liquid form add the hot content from china dish W2 from the china dish W1 and stir the content continuously.
7. Now take out the mould from the refrigerator and pour all the content in the suppository mould see below picture the mould is filled with content now this will be place again in the refrigerator.

Fig 7
Filled suppositories

4) After some time, the suppositories are removed out from the refrigerator and the suppositories formed as below.

Formed suppositories Fig 8

Evaluation Test

Fig 9

1. Appearance test

- It is a mixture of glycerine and water which is made stiff by the addition of gelatin
- The suppository when cut longitudinally and examined with the naked eye the internal and external surface of suppository should be uniform in appearance
- Compliance with the standard indicate satisfactory subdivision and dispersion of suspended material
- Colour- slightly yellow, Translucent and Transparent
- Nature- Soft to touch

2. Solidification time

- Solidification time of 20 suppositories is 3 hr. and 15 min.
- There is relationship between melting and solidification that is important to characterise
- The release of the active ingredient from the vehicle is related to the melting point of the vehicle and the solubility of the drug in the vehicle

- Suppositories undergoes three changes in their phase during their life. First they are melted and then solidify; upon administration, they are again melted and understanding of these factor and their relationship is critical for evaluating the by availability of the final suppositories formulation.
- The higher the melting point the later the drug effect appears. If too high the drug effect does not appear.
- The solidification temperature is define as the highest temperature occurring during the solidification of a supercool liquid

Melting range test

- This test also called the macro melting range test and is a major of the time it takes for the entire suppository to melt when immersed in a constant temp. 37degree Celsius water bath.
- In contrast micro melting range test in the melting range measured in capillary tube for the fat base only the apparatus commonly use for the measuring the melting range of the entire suppository in is a USP tablet disintegration apparatus
- The suppository is completely immersed in the constant water bath and the time for the entire suppository to melt or disperse in the surrounding water is measure 2 to 3 min.

Uniformity of weight variation

- When 20 suppositories individually w1, w2, w3, w20.
- Weigh all the suppositories together = W
- Calculate the average weight = W/20

W1= 1.14	W9 = 1.15	W17 =1.14
W2= 1.12	W10 =1.10	W18 =1.19
W3= 1.14	W11 = 1.14	W19 = 1.16
W4= 1.18	W12 =1.11	W20 =1.02
W5=1.16	W13 =1.17	
W6=1.14	W14 =1.19	
W7=1.13	W15 =1.02	
W8=1.17	W16 =1.13	

Table.4

W= W1+W2+W3+W4+……W20/20
1.14+1.12+1.14+1.18+1.16+1.14+1.13+1.07+1.15+1.10+1.14+1.11+1.17+1.19+1.02+1.13+1.14+1.19+1.16+1.02 /20

W= 1.13
Limits for uniformity of weight variation –
Limit 1. Not more the 2 suppositories differ from the average weight by more than 5 per.
Therefore, upper limit = average weight +5. Average weight / 100
1.13+ 1.13 x 5/100= 1.1865
Lower limit = average weight – 5. average weight /100
1.13-1.13 x5 /100 = 1.08.

By observing fig no 1 not more than 2 suppository deviates from the average weight by 5%

Limit 2. Not more than 2 of the suppositories differ from the average weight by more than the percent error listed
If more than 2 suppositories are different from the average weight by 5 per.

Calculate double the percent error as follows

Therefore, upper limit = average weight + 10. Average weight/100
=1.13+ 1.13x10/100
= 1.24

Lower limit average weight – 10. Average weight/100
= 1.13-1.13 x 10/100
=1.02

By observing fig.no 1 no suppository deviates from the average weight by then 10 % If the weight is found to be too small it is advisable to check whether the mould is being well filled and whether there are axial cavities or air bubbles cause by badly adjusted mechanical stirring or the presence of an undesirable surfactants.
It is important to check that the batch of suppositories if homogenous
If the weight is found to be high check that scrapping has been carried out correctly and also that the mixture is homogenous

The weight may decrease during ageing when the suppositories confirm volatile substances specially if the packaging is not airtight.

RESULT:

1) In the appearance test of the glycerogelatin suppositories colour is found as slightly yellow, translucent and soft to touch in nature.
2)In the melting range test of glycerogelatin suppositories are melted at constant temperature 37degree Celsius within 2 to 3 min.
3)The solidification time of the glycerogelatin suppositories was found to be 3 hr 15 min.
4)Uniformity of weight variation test we take the average weight of 20 suppositories.
1.Not more than 2 suppository deviates from the average weight by more than 5%.
2.Not suppository was found to be deviate from the average weight by more than 10%.

CONCLUSION:

As per the present study shows the preparation for formulation and evaluation of glycerogelatin suppository in which we can firstly make a formulation for 20 suppositories which contain the ingredient liquid paraffin, lactic acid 0.2g gelatin1.47g glycerol 6.86g and distilled water 147 or quantity sufficient added then after the formulation of suppositories we had place the suppository mould in the refrigerator then calculate the solidification time of glycerogelatin suppositories is 3hr 15min. after the solidification we had perform the evaluation test for glycerogelatin suppository like appearance test -In appearance test we can check the colour and nature of glycerogelatin suppository The melting range test is also performed to check the melting time of suppository at which temperature suppository get melt 37degree Celsius suppository get melted. And then also the uniformity of weight variation is also conducted to check the content of average weight of each suppository after the formulation and evaluation of suppository we can storied the suppository of the optimum temperature. `

REFERENCES:

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7877752/
2. https://www.tandfonline.com/doi/abs/10.1179/joc.2009.21.3.243
3. https://epublications.marquette.edu/cgi/viewcontent.cgi?article=1460&context=nursing_fac
4. https://en.m.wikipedia.org/wiki/Suppository
5. https://www.sciencedirect.com/science/article/pii/S0923250817300839
6. https://solutionpharmacy.in/preparation-of-suppositories/
7. https://www.researchgate.net/figure/Different-shapes-and-sizes-of-suppositoriesdesigned-in-CURA-Solidworks-in-combination_fig1_333023523
8. https://www.interchim.fr/ft/Q/Q45850.pdf
9. http://pharmich.blogspot.com/2016/02/displacement-values.html?m=1
10. https://eduwavepool.unizwa.edu.om/lmsdatapool/00010148/LearningObjects/practical.d oc
11. https://uomustansiriyah.edu.iq/media/lectures/4/4_2020_04_24!05_48_49_PM.docx
12. http://eacademic.ju.edu.jo/l.tutunji/Material/Topic%209-%20suppositories.ppt
13. https://www.pharmaguideline.com/2021/10/methods-of-preparation-displacementvalue-calculation-evaluation-of-suppositories.html
14. https://pubchem.ncbi.nlm.nih.gov/compound/Lactic-acid
15. https://en.wikipedia.org/wiki/Lactic_acid
16. https://patents.google.com/patent/EP2130531A1/en
17. https://www.mjpms.in/
18. https://www.sciencedirect.com/
19. https://agris.fao.org/
20. https://thepharmapedia.com/
21. https://www.nature.com/articles/s41522-022-00295-y