INTRODUCTION

After exploration of the importance of Probiotic microorganisms like Lactobacillus species, Bifidobacterium species and their importance for "Human Gut Lumen Microbiota" and for "Skin Microbiota", scientific work upon this field is growing in an exponential manner. Because of the importance of probiotics for gut microbiota, and the importance of gut microbiota for human health and the immune system, probiotics attract the attention of many groups [1-10]. Different articles report interesting results, i.e. anti-cancer properties of bioactive peptides from symbiotic yogurt [5], antibacterial activity of bacteriocin isolated from lactobacillus bulgaricus [6], one article contemplates the probiotics as undervalued conquerors [8], one review article reports about the anti-aging properties of probiotics [9], another article reports about the role of gut microbiota in lipid metabolism, cholesterol levels and the positive effect of probiotics in infants with atopic dermatitis [10]. Since yogurt also contains probiotics, it can eventually be an important candidate as an excipient for various topical dermatological products. As an example of utilizing yogurt as a major excipient for topical dermatological products, we are working on a topical ointment using yogurt as one of the main excipients, in excess of 50%. Besides yogurt, Dexpanthenol, Olive Oil, Almond Oil and other necessary ingredients for emulsion formation and antimicrobial agents are being used. The resulting ointment has acceptable organoleptic, microbiological, physical-chemical properties and stability (unpublished results). It has been reported by different authors, that probiotic bacteria are lysed by heat at elevated temperatures (70-100 °C). Following the lysis of probiotic bacteria, favorable cell contents for the skin microbiome, including Antimicrobial Peptides (Bacteriocins) are excreted [4-6]. Recent studies report that Antimicrobial Peptides (Bacteriocins) are also present in yogurt, which seem to be stable at elevated temperatures, i.e. 80 °C [6]. It has also been shown by different publications and patents that the "lysates" of probiotics are at least as effective as their "live" forms in inhibiting various pathogenic bacteria, either in the gut lumen and/or skin surface [7, 11-14]. The conventional method of manufacturing topical dermatological products is performed at elevated temperatures (i.e. 80 °C) and under turbulent homogenization. Considering the fact that probiotic bacteria would be lysed at elevated temperatures, it is highly probable that the probiotics in yogurt, when yogurt is used as an excipient for topical dermatological products, should also be in the lysed form following the production of the corresponding ointment. Besides, the added antimicrobial agents would also be contributing to this lysation process. Not to be forgotten is the fact that yogurt is not only rich in probiotics. Besides probiotic bacteria, yogurt is rich in Amino Acids (amino acids make up 40% of the skin’s Natural Moisturizing Factor/NMF [15], Vitamins, Fatty Acids, and Minerals [16]. It can be assumed that only very small fractions of Amino Acids, Vitamins, Fatty Acids and Minerals will reach the skin surface following systemic application of these ingredients in various dosage forms. In case the skin, i.e. the Stratum Corneum is directly targeted, yogurt could eventually be used as an excipient for various topical dermatological products, for supplying the skin with; Lysed Probiotic Bacteria, Amino Acids, Vitamins, Fatty Acids and Minerals, locally. It seems as if there is quite some work to be done upon this field.

Hypothesis

Yogurt

The word "yogurt" is a Turkish word. It is believed to have come from the word “yogurmak” which means to thicken, coagulate and curdle [17, 18]. Yogurt is a fermented milk product. Following fermentation, the main structure of yogurt consists of a casein gel. In between, there are empty spaces filled with a liquid phase known as whey, which is the liquid part of milk left after fermentation. Some of these spaces are filled with starter bacteria [1]. The main starter cultures/bacteria which are used for the production of yogurt are; "Streptococcus thermophilus" and "Lactobacillus bulgaricus". S. thermophilus is an aerobic and L. bulgaricus an anaerobic bacterium [1, 2, 17, 18]. Both bacteria cooperate for the fermentation of milk. As a result, from lactose in milk, lactic acid is produced. The pH will be more acidic, where the growth of other bacteria is unfavorable. During this cooperation, S. thermophilus produces pyruvic acid, formic acid and carbon dioxide, which in turn stimulate the growth of L. bulgaricus. L. bulgaricus produces peptides and amino acids which promote the growth of S. thermophilus [19]. According to...
FAO/WHO, these two bacteria fulfill the definition of probiotic bacteria. FAO/WHO defines Probiotics as “live microorganisms, which when administered in adequate amounts, confer a health benefit on the host” [3]. According to Guarner et al. [20], taken here “word by word” from the corresponding publication; “a number of human studies have clearly demonstrated that yogurt containing viable bacteria (Streptococcus thermophilus and Lactobacillus delbrueckii sp. Bulgaricus) improve lactose digestion and eliminate symptoms of lactose intolerance. Thus, these cultured bacteria clearly fulfill the current concept of probiotics”.

FDA/WHO define probiotics as “live microorganisms, which when administered in adequate amounts, confer a health benefit on the host” [3]. According to Guarner et al. [20], taken here “word by word” from the corresponding publication; “a number of human studies have clearly demonstrated that yogurt containing viable bacteria (Streptococcus thermophilus and Lactobacillus delbrueckii sp. Bulgaricus) improve lactose digestion and eliminate symptoms of lactose intolerance. Thus, these cultured bacteria clearly fulfill the current concept of probiotics”.

USDA National Nutrient Database for Standard Reference [16], has reported the nutrient composition of "Plain Yogurt/Whole Milk" in its "4/1/2019 Release". The relevant nutrients, excluding the ones under the title "Others", are presented in table 1. Besides nutrients, yogurt contains probiotics like “S. thermophilus” and “L. bulgaricus”. Antimicrobial Peptides (Bacteriocins) are also identified in yogurt, which seems to be stable at elevated temperatures, i.e. 80 °C [4-6].

### Table 1: Nutritional value of plain, whole milk yogurt. From USDA. Composition of Yogurt/nutrients in 100g

| Proximates | 100g | Amino acids | 100g | Reference |
|------------|------|-------------|------|-----------|
| Water      | 87.90g | Tryptophan  | 0.020g | [16]      |
| Protein    | 3.47g  | Threonine   | 0.142g |           |
| Total Lipid (Fat) | 3.25g | Isoleucine  | 0.109g |           |
| Carbohydrate | 4.66g | Leucine     | 0.350g |           |
| Sugars     | 4.66g  | Lysine      | 0.311g |           |
| Minerals   | 100g  |             |       |           |
| Calcium, Ca| 0.51g  | Phenylalanine | 0.109g |           |
| Iron, Fe   | 0.05g  | Tyrosine    | 0.175g |           |
| Magnesium, Mg | 12 mg | Valine      | 0.287g |           |
| Phosphorus, P | 95 mg | Arginine    | 0.104g |           |
| Potassium, K| 155 mg | Histidine  | 0.086g |           |
| Sodium, Na | 46 mg  | Alanine     | 0.148g |           |
| Zinc, Zn   | 0.57 mg | Aspartic acid | 0.275g |           |
| Copper, Cu | 0.009 mg | Glutamic acid | 0.679g |           |
| Manganese, Mn | 0.004 mg | Glycine | 0.084g |           |
| Selenium, Se | 2.2µg | Proline     | 0.411g |           |
| Fluoride, F | 12µg   | Serine      | 0.215g |           |

### Vitamins

| 100g | Lipids | 100g |
|------|--------|------|
| Vit C (total Ascorbic acid) | 0.5 mg | Fatty acids, total saturated | 2.096g |
| Thiamin, Vit B1 | 0.029 mg | 4:0 | 0.096g |
| Riboflavin | 0.142 mg | 6:0 | 0.066g |
| Niacin | 0.075 mg | 8:0 | 0.042g |
| Panthotenic acid | 0.389 mg | 10:0 | 0.093g |
| Vit B6 | 0.032 mg | 12:0 | 0.111g |
| Folate Total | 7 µg | 14:0 | 0.343g |
| Folate beta | 5 µg | 16:0 | 0.386g |
| Choline Total | 15.2 mg | 18:0 | 0.317g |
| Vit B12 | 0.37 µg | Fatty acids, total monounsaturated | 0.893g |
| Retinol | 27 µg | 16:1 | 0.071g |
| Vit A, RAE | 27 µg | 18:1 | 0.743g |
| Vit E, (alpha-tocopherol) | 0.06 µg | 20:1 | 0 |
| Vit D (D2+D3) | 0.14 µg | 22:1 | 0 |
| Vit D3 (cholecalciferol) | 0.14 µg | 22:1 | 0 |
| Vit D | 2 IU | Fatty acids, total polyunsaturated | 0.092g |
| Vit K (phyloquinone) | 0.24 µg | 18:2 | 0.065g |
|          |       | 18:3 | 0.027g |
|          |       | 18:4 | 0 |
|          |       | 20:4 | 0 |
|          |       | 20:5 n-3 (EPA) | 0 |
|          |       | 22:5 n-3 (DPA) | 0 |
|          |       | 22:6 n-3 (DHA) | 0 |
|          |       | Cholesterol | 13 mg |

**Considering yogurt as an excipient for various topical dermatological products from the aspect of amino acids, vitamins, and minerals**

As an example of utilizing yogurt as an excipient for topical dermatological products, we are working on a topical ointment using yogurt as the main excipient, in excess of 50%. Besides Yogurt, Dexpanthenol, Olive Oil, Almond Oil, and Antimicrobial Agents, other necessary ingredients for emulsion formation are being used. The resulting ointment has acceptable organoleptic, physical-chemical, microbiological properties and stability (unpublished results). For the sake of simplicity, let us consider that we use, besides other necessary ingredients for emulsion formation and antimicrobials, 50%/50g yogurt in a 100g ointment. We can then, depending on table 1, calculate the amount of amino acids, vitamins, minerals and lipids which would be present in such a formulation (excluding the lipids coming from the other ingredients). In table 2, the amount of nutrients in 50g yogurt are also calculated depending on the data of USDA [16]. Since we aim at using 50%/50g yogurt in our hypothetical formulation, the nutrients which are present in 50g yogurt should be present in our 100g hypothetical formulation. In our preliminary studies, we were able to reassess the amount of amino acids in our finished topical formulation, which was proportional to the amounts of amino acids in the yogurt sample.
used (unpublished results). We have “not” done similar studies for the vitamins, minerals and lipids. In the corresponding columns of table 2, depending on the data of USDA [16], the amount of amino acids, minerals, vitamins, and lipids which would be present in 1g of the above mentioned hypothetical 100g ointment are calculated. 1g ointment also corresponds to 2 Finger Tip Units (FTU). The details for FTU for an adult male fingertip is given below [21]:

Table 2: Amount of nutrients in 50g yogurt and in 1g (2 FTU) of a hypothetical ointment containing 50%/50g yogurt. The amounts are calculated depending on the yogurt data of USDA, from table 1

| Minerals | 50g | 1g Ointment (2 FTU) | Amino acids | 50g | 1g Ointment (2 FTU) | Reference |
|----------|-----|---------------------|-------------|-----|---------------------|-----------|
| Calcium, Ca | 60.5 mg | 60.5µg | Tryptophan | 0.010g | 100µg | [16] |
| Iron, Fe | 0.025 mg | 0.25µg | Threonine | 0.71g | 7100µg |
| Magnesium, Mg | 6 mg | 60µg | Isoleucine | 0.0945g | 945µg |
| Phosphorus, P | 47.5 mg | 475µg | Leucine | 0.175 | 1750µg |
| Potassium, K | 77.5 mg | 775µg | Lysine | 0.1555g | 1555µg |
| Sodium, Na | 23 mg | 230µg | Methionine | 0.051g | 510µg |
| Zinc, Zn | 0.295 mg | 2.95µg | Cystine | 0.016g | 160µg |
| Copper, Cu | 0.0045 mg | 0.045µg | Phenylalanine | 0.0945g | 945µg |
| Manganese, Mn | 0.002 mg | 0.02ug | Tyrosine | 0.0875g | 875µg |
| Selenium, Se | 1.1 µg | 11µg | Valine | 0.1435g | 1435µg |
| Fluoride, F | 6 µg | 60µg | Arginine | 0.052g | 520µg |
| Vitamins | 50g | 1g Ointment (2 FTU) | Histidine | 0.043g | 430µg |
| Vit B12 | 0.0045 mg | 0.045µg | Alanine | 0.074g | 740µg |
| Thiamin, Vit B1 | 0.0145 mg | 0.145µg | Aspartic acid | 0.1375g | 1375µg |
| Riboflavin | 0.071 mg | 0.71µg | Glutamic acid | 0.3395g | 3395µg |
| Niacin | 0.0375 mg | 0.375µg | Glycine | 0.042g | 420µg |
| Panthotenic acid | 0.1945 mg | 1.945µg | Proline | 0.2055g | 2055µg |
| Vit B6 | 0.016 mg | 0.16µg | Serine | 0.1075g | 1075µg |
| Folate Total | 3.5 µg | 0.35µg | Fatty acids, total saturated | 1.048g | 10480µg |
| Folic acid | 0 | 0 | 4:0 | 0.048g | 480µg |
| Choline | 7.6 mg | 76µg | 6:0 | 0.033g | 330µg |
| Vit B12 | 0.185 µg | 0.00185µg | 8:0 | 0.021g | 210µg |
| Retinol | 13.5 µg | 0.135µg | 10:0 | 0.0465g | 465µg |
| Vit A, IU | 49.5 IU | 0.495 IU | 12:0 | 0.0555g | 555µg |
| Vit A (alpha-tocopherol) | 0.035 mg | 0.35ug | 14:0 | 0.1755g | 1755µg |
| Vit D (D2+D3) | 0.055µg | 0.055µg | 16:0 | 0.443g | 4430µg |
| Vit D3 (cholecalciferol) | 0.05µg | 0.05µg | 18:0 | 0.1585g | 1585µg |
| Vit D | 1 IU | 0.01 IU | Fatty acids, total monounsaturated | 0.4465g | 4465µg |
| Vit K (phyllquinone) | 0.1 µg | 0.01µg | 16:1 | 0.0355g | 355µg |
| Cholesterol | 6.5 mg | 65µg | 18:1 | 0.3715g | 3715µg |
| | | | 18:2 | 0.0325g | 325µg |
| | | | 18:3 | 0.0135g | 135µg |
| | | | 18:4 | 0.0125g | 125µg |
| | | | 20:4 | 0.0125g | 125µg |
| | | | 20:5 n-3 (EPA) | 0 | 0 |
| | | | 22:5 n-3 (DPA) | 0 | 0 |
| | | | 22:6 n-3 (DHA) | 0 | 0 |
| | | | Cholesterol | 6.5 mg | 65µg |

The quantity of cream in a Finger Tip Unit (FTU) varies with age [21]:
- Adult male: 1 finger-tip unit provides 0.5g
- Trunk, front and back: 14 FTU
- Entire body: about 40 FTU

The necessary FTU for different body areas are given below [21]:
- Adult male: 1 finger-tip unit provides 0.5g
- Trunk, front and back: 14 FTU
- Entire body: about 40 FTU

We would then need 2 FTU=1g ointment, as expressed above. The corresponding amount of nutrients that would be delivered by the hypothetical 1g ointment are shown in table 2.
Questions about the fraction of an amino acid dose reaching the *stratum corneum* following systemic application

Amino acids are, among others, breakdown products of *filagrin* which is important for proper epidermal differentiation and skin barrier function.

The amino acids and the other byproducts of *filagrin* contribute to the formation of the *Natural Moisturizing Factor (NMF)* [22] as shown in Table 3 [15]. The Confocal Raman Spectroscopy depth measurements indicate that the *NMF* concentration is higher in the whole *Stratum Corneum* of the human skin [23].

| Free Amino Acids                        | 40%     | Reference [15] |
|----------------------------------------|---------|----------------|
| Pyrrolidone carboxylic acid            | 12%     |                |
| Lactate                                | 12%     |                |
| Sugars                                 | 8,5%    |                |
| Urea                                   | 7%      |                |
| Chloride                               | 6%      |                |
| Sodium                                 | 5%      |                |
| Potassium                              | 4%      |                |
| Ammonia, uric acid, glucosamine and creatine | 1,5%       |                |
| Calcium                                | 1,5%    |                |
| Magnesium                              | 1,5%    |                |
| Phosphate                              | 0,5%    |                |
| Citrate, formate                        | 0,5%    |                |

As far as our surveys about the data in the scientific literature are concerned, we do not know what fraction of a systemically applied amino acid dose would reach the *Skin/Stratum Corneum*. For many drugs, the term Volume of Distribution (pharmacokinetics) is used as a calculation factor to approximately calculate the amount of drug in the body at any time, by making use of i.e. plasma concentrations. As an example, let us take the Volume of Distribution of the amino acid *Arginine*, which is given to be around 24 liters, assessed in humans. The authors [24] have infused 3g of L-Arginine to humans and have measured “peak plasma concentrations” of approximately 400 µmoles/liter, which corresponds to approximately 70µg/ml for L-Arginine.

The U. S. Food and Nutrition Board has published the Recommended Dietary Allowances for various amino acids for adults. Depending on the type of amino acid, the amounts vary between 8-14 mg per kg of body weight [25]. If we consider an average value of 10 mg/kg allowance for a certain amino acid, for an average person of 75 kg body weight, the total dietary allowance would be around 0,75g. As cited above, after an infusion of 3g L-Arginine, the peak plasma concentrations are measured to be approximately 70µg/ml [24]. After systemic application of 0,75g amino acid, the plasma concentrations should be considerably lower (assuming 100% bioavailability and no "first-pass-effect" following peroral application). It can be assumed that only very small fractions of the amount present in the plasma would reach the Skin Surface/ *Stratum Corneum*.

Looking at Table 2, it can be seen that relative significant amounts of amino acids can be delivered locally to the *stratum corneum* by utilization of yogurt as an excipient in a topical dermatological product.

Amino acids make up 40% of the skin’s *Natural Moisturizing Factor/NMF*. The other constituents of the NMF besides amino acids are given in Table 3 [15]. One could eventually achieve significant moisturization of the skin by delivering amino acids, minerals, and the humectant lactic acid (which is one of the major constituents of yogurt) by means of a topical yogurt containing ointment locally.

As shown in Table 1, besides amino acids, yogurt also contains significant amounts of vitamins, minerals, and lipids. We have not studied the fate and proportional transfer of vitamins, minerals, and lipids from the yogurt samples used. They may or may not have been degraded during the manufacturing process. There seems to be quite some work to be done upon this field.

**Considering yogurt as an excipient for topical dermatological products from the aspect of *lived probiotics***

**The skin Microbiome**

Since the *Skin Microbiome* is the main scope of this paper, various other *Microbiomes* of the human body will not be discussed.

In their very interesting paper, Grice and Segre [26], have presented the schematic of the skin histology in a cross-sectional form. Microorganisms, like viruses, bacteria, and fungi are schematized on the surface of the skin, which also reside in sweat glands, *sebaceous glands*, hair and hair shaft. Rod-shaped and round bacteria, like *Propionibacterium* and *Staphylococcus spp.*, commensal fungi like *Malassezia spp.* and skin mites (i.e. *Demodex folliculorum*, *Demodex brevis*) are also schematized for the reader in a brilliant and very understandable scheme. All these microorganisms live in communities and in close association with each other. Major examples of the *19 phyla* which are known to be part of the skin microbiome are; *Actinobacteria* (51, 8%), *Firmicutes* (24, 4%), *Proteobacteria* (16,5%) and *Bacteroidetes*. The major genera are *Corynebacterium, Propionibacterium*, and *Staphylococcus* [27]. The skin is an ecosystem of, microorganisms and host, existing in balance and harmony. The disturbance of this *homeostasis* may lead to different diseases [26, 27]. On the other hand, this *homeostasis* may also be misbalanced by *exogenous* agents, used for the treatment of various dermatological disorders. This should perhaps lead us to re-evaluate our understanding of treating various diseases, i.e. the unnecessary use of antibiotics, which may disturb the *microbiome* balance and harmony, resulting in *dysbiosis*. In such cases, it may take long periods for the *microbiome* to recover [27, 28].

**Use of *lysed probiotics* and their effect on the skin**

It has been shown by different publications and patents that the "lysedes" of *probios* are at least as effective as their "live" forms in inhibiting various *pathogenic* bacteria, either in the Gut Lumen and/or Skin Surface [7, 11-14, 29, 30].

Since it is not the scope of this paper to discuss the effects of "live probiotics" on the skin *microbiome*, solely the effect of "lysed probiotics" will be discussed. As already implemented above, FAO/WHO defines *Probiotics* as; "live microorganisms, which when administered in adequate amounts, confer a health benefit on the host" [3]. According to Guarner et al. [20], taken here from the corresponding publication "word by word"; "a number of human studies have clearly demonstrated that yoghurt, containing viable *Bacteroides* (51, 8%), *Firmicutes* (24, 4%), *Propionibacterium* (16,5%) and *Bacteroidetes*. The major genera are *Corynebacterium, Propionibacterium*, and *Staphylococcus* [27]. The skin is an ecosystem of, microorganisms and host, existing in balance and harmony. The disturbance of this *homeostasis* may lead to different diseases [26, 27]. On the other hand, this *homeostasis* may also be misbalanced by *exogenous* agents, used for the treatment of various dermatological disorders. This should perhaps lead us to re-evaluate our understanding of treating various diseases, i.e. the unnecessary use of antibiotics, which may disturb the *microbiome* balance and harmony, resulting in *dysbiosis*. In such cases, it may take long periods for the *microbiome* to recover [27, 28].

Pique et al. mention different methods for the inactivation/lysisation of *probiotic* bacteria. The mentioned methods are; heat (70–100 °C), chemicals like formalin, gamma or ultraviolet rays and sonication. The preferred method being heat inactivation. Inactivation ruptures the cell walls of the *probiotic* bacteria, thereby releasing the cytoplasmic contents, i.e.; DNA and cell wall components like Peptidoglycans, Lipoteichoic acids or heat-labile *Pili*. They cite that the excreted components play key immunomodulating roles, i.e.
production of IgA by "S. thermophilus lysates" and anti-inflammatory responses mediated by metabolites and cell surfaces of "L. delbrueckii". The authors cite that the lysate components of heat-killed probiotics would inhibit pathogens and also release Antimicrobial Peptides (Bacteriocins) which are effective against Gram-positive and Gram-negative bacteria [11]. Lew and Liang cite that the cell wall fragments of probiotic bacterial extracts, their metabolites and the dead probiotic bacteria as such, can improve skin barrier functions and regulate immune responses. One of the components of lysed S. thermophilus, the Sphinogomelysin enzyme, when applied in cream was able to increase the ceramide levels on the volar forearm of healthy human volunteers significantly (p<0.05) within a week. Other cell components, like Lipoteichoic acid, increases dermal cellular defense against bacterial infection and Peptidoglycan plays an important role in defending the skin against pathogens [12].

Shigwedha et al. name the "probiotic cell fragments (PCFs)" of probiotics as "parabiotics" since they do not represent intact bacteria. They also cite that the cell components of such bacteria, i.e. Peptidoglycan, Lipoteichoic acid, cell wall-associated Polysaccharides, Muramyl peptide, Muramyl dipeptide, when applied intestinally would exert beneficial effects. They mention that these cell fragments inhibit the adhesion of C. perfringens, E. coli, S. thyphimurium, C. difficile, Shigella sp. and Salmonella sp. to mucus and/or intestinal epithelial cells in a competitive way [7].

Di Marzio et al. have shown that sonicated (lysed) S. thermophilus strains, "which is one of the starter cultures for yogurt", when applied topically to patients suffering from atopic dermatitis, increased the level of ceramides in the stratum corneum thereby improving barrier function [29].

In one patent application [30], the inventors describe the use of lysed probiotic bacteria against skin infections. Lysates of Lactobacillus rhamnosus GG, was shown to inhibit Staphylococcus aureus infection by preventing the adhesion of S. aureus to cells. They also cite that these lysates can be administered in different dosage forms, including liposomes and other microparticulate dosage forms.

In a thesis submitted to the University of Manchester Medical Faculty, it is cited that lysates of Lactobacillus rhamnosus GG was effective against the adhesion of S. aureus to keratinocytes thereby counteracting infections. It has also been shown that L. rhamnosus GG lysates also enhance the re-epithelization of wounds, favoring keratinocyte terminal differentiation. The study cites that L. rhamnosus GG lysates can be used as a therapeutic agent to enhance wound healing [13].

Guénniche et al., cite that lysates of Bifidobacterium longum spp. would improve sensitive skin. Skin sensitivity was assessed by the stinging test. Following barrier disruption, skin recovery was evaluated by measuring the Trans-Epidermal Water Loss (TEWL), in a double-blind, randomized, placebo-controlled trial, where a 10% cream of B. longum spp. lysate was applied. The results show that the volunteers who used the extract in a cream form had a significant drop in skin sensitivity and a significant decrease in skin dryness at the end of the treatment [14].

Tufail et al., isolated Bacteriocins (Antimicrobial Peptides) from Lactobacillus bulgaricus (which is one of the starter cultures of yogurt) and tested the inhibitory activity against B. subtilis, E. coli, S. typhi, St. aureus, V. cholerae by use of the agar diffusion method. They cite that the isolates have antibacterial potential against the mentioned pathogens [6].

To give the reader a picture about the amount of "L. bulgaricus and S. thermophilus" in yogurt, which are the main probiotics (starter bacteria) for yogurt production, the viable bacterial counts in yogurt are given below in table 4.

### Table 4: The viable bacterial counts in Yogurt [2, 31]

| Authors | Reference |
|---------|------------|
| Yilmaz-Ersan I, Kural D. | [2] |
| S. thermophilus | 9.01 (log cfu/ml) |
| L. bulgaricus | 8.42 (log cfu/ml) |
| Sarvari F, Mortazavian AM, Fazeli MR | [31] |
| S. thermophilus | 8.72 (log cfu/ml) |
| L. bulgaricus | 8.46 (log cfu/ml) |

### CONCLUSION

The utilization of yogurt as an excipient for various topical dermatological products is discussed. If such an ointment, where yogurt is used as an excipient, is manufactured by conventional methods (elevated temperatures and turbulent homogenization), under such conditions the major probiotic bacteria used for yogurt production (in this case S. thermophilus and L. bulgaricus) should be in the lysed state following the production of the ointment. In addition to heat and turbulent homogenization, the added antimicrobial agent(s) would also support this lysisation process.

Many groups have shown that "lysed probiotics" exert favorable effects on the skin. These effects were shown to be at least as favorable as the "live forms" of the corresponding probiotics. Apart from using S. thermophilus and L. bulgaricus as starter cultures for yogurt production, different probiotics (starter cultures) may also be used. The corresponding yogurt samples (with different starter cultures) could perhaps be used in ointments, depending on the targeted effect to be achieved. Using yogurt as an excipient for a certain topical dermatological product could be promising for the future, since such a formulation may deliver significant amounts of; "Lysed Probiotics", "Amino Acids (amino acids make up 40% of the skin’s Natural Moisturizing Factor/NMF)", "Vitamins and fatty acids (it needs to be assessed whether the vitamins and the fatty acids are transferred from yogurt to the final formulation without degradation)" and "Minerals" to the Stratum Corneum locally.

### OVERVIEW

The utilization of yogurt as an excipient for various topical dermatological products is discussed. Yogurt contains live probiotics as such, which are shown to be exerting favorable effects in the human body. On the other hand, as cited in the above text, many groups have also shown that "lysed probiotics" also exert favorable effects in the human body and the skin locally. Using yogurt as an excipient for a certain topical dermatological product could be promising, since such a formulation may also deliver significant amounts of; Lysed Probiotics, Amino Acids (amino acids make up 40% of skin’s Natural Moisturizing Factor/NMF), Fatty Acids, Minerals and Vitamins to the stratum corneum locally. We were able to reassess the proportional corresponding amounts of amino acids in the final topical formulation that were present in the yogurt samples used (unpublished results). But no further studies were done in order to determine if all the Vitamins and Fatty Acids in the yogurt sample are transferred to the ointment intact, without degradation. Further studies are needed in order to investigate the utilization of yogurt as an excipient in topical dermatological products and its corresponding clinical implications.

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### AUTHORS CONTRIBUTIONS

All the authors have contributed equally.
CONFLICT OF INTERESTS
The author reports no conflict of interest.

REFERENCES
1. De Vuyst L, Degeet B. Heteropolysaccharides from lactic acid bacteria. FEMS Microbiol Rev 1999;23:153-77.
2. Yilmaz Ersan L, Kurald E. The production of set-type-bio-yoghurt with commercial probiotic culture. Int J Chem Eng Appl 2014;5:402-8.
3. Report of a joint food and agriculture organization of the United Nations/World Health Organization (FAO/WHO) expert consultation on the evaluation of health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria. Cordoba, Argentina; 2001.
4. Mohanty D, Ray P. Evaluation of probiotic and antimicrobial properties of Lactobacillus bulgaricus strains isolated from dairy products. Int J Pharm Sci 2016;8:92-30.
5. Sah BNP. Identification of bioactive peptides produced by symbiotic yogurt having anti-cancer properties. A thesis submitted for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.
6. Tufail M, Hussain S, Malik F, Mirza T, Parveen G, Shafaat S. Isolation and evaluation of antibacterial activity of bacteriocin produced by lactobacillus bulgaricus from yogurt. Afr J Microbial Res 2011;5:3842-7.
7. Shigwedha N, Sichel L, Jia L, Zhang L. Probiotic cell fragments (PCFs) as novel nutraceutical ingredients. J Biosci Med Probiotical
8. 2014;2:43-55.
9. Kawatra P, Aliypapa C. Probiotics: the undervalued conquerors. Asian J Pharm Clin Res 2015;8:97-100.
10. Sivamathurth SB, Kesika P, Chaiyasat C. A review of anti-aging properties of probiotics. Int J Appl Pharm 2018;10:23-7.
11. Kvit K, Kharchenko V. Role of gut microbiota in lipid metabolism. Asian J Pharm Clin Res 2018;11:1-4-8.
12. Pique N, Berlanga M, Minana Galbis D. Health benefits of heat-killed (tyndallized) probiotics: an overview. Int J Mol Sci 2019;20:1-30.
13. Lew LC, Liong MT. Bioactives from probiotics for dermal health: functions and benefits. J Appl Microbiol 2013;114:1241-53.
14. Mohammad Saeed W. Characterisation of the potential of probiotics or their extracts as therapy for skin. A thesis submitted to the University of Manchester for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.
15. Gueniche A, Bastien P, Ovigne JM, Kermici M, Courchay G, Sciences; 2014.
16. Pique N, Berlanga M, Minana Galbis D. Health benefits of heat-killed (tyndallized) probiotics: an overview. Int J Mol Sci 2019;20:1-30.
17. Lew LC, Liong MT. Bioactives from probiotics for dermal health: functions and benefits. J Appl Microbiol 2013;114:1241-53.
18. Mohammad Saeed W. Characterisation of the potential of probiotics or their extracts as therapy for skin. A thesis submitted to the University of Manchester for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.
19. Gueniche A, Bastien P, Ovigne JM, Kermici M, Courchay G, Sciences; 2014.
20. Pique N, Berlanga M, Minana Galbis D. Health benefits of heat-killed (tyndallized) probiotics: an overview. Int J Mol Sci 2019;20:1-30.
21. Dissolution of lactic acid bacteria. Cordoba, Argentina; 2001.
22. Tufail M, Hussain S, Malik F, Mirza T, Parveen G, Shafaat S. Isolation and evaluation of antibacterial activity of bacteriocin produced by lactobacillus bulgaricus from yogurt. Afr J Microbial Res 2011;5:3842-7.
23. Sah BNP. Identification of bioactive peptides produced by symbiotic yogurt having anti-cancer properties. A thesis submitted for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.
24. Kvit K, Kharchenko V. Role of gut microbiota in lipid metabolism. Asian J Pharm Clin Res 2018;11:1-4-8.
25. Pique N, Berlanga M, Minana Galbis D. Health benefits of heat-killed (tyndallized) probiotics: an overview. Int J Mol Sci 2019;20:1-30.
26. Lew LC, Liong MT. Bioactives from probiotics for dermal health: functions and benefits. J Appl Microbiol 2013;114:1241-53.
27. Mohammad Saeed W. Characterisation of the potential of probiotics or their extracts as therapy for skin. A thesis submitted to the University of Manchester for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.
28. Gueniche A, Bastien P, Ovigne JM, Kermici M, Courchay G, Sciences; 2014.
29. Pique N, Berlanga M, Minana Galbis D. Health benefits of heat-killed (tyndallized) probiotics: an overview. Int J Mol Sci 2019;20:1-30.
30. Lew LC, Liong MT. Bioactives from probiotics for dermal health: functions and benefits. J Appl Microbiol 2013;114:1241-53.
31. Mohammad Saeed W. Characterisation of the potential of probiotics or their extracts as therapy for skin. A thesis submitted to the University of Manchester for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.
32. Dissolution of lactic acid bacteria. Cordoba, Argentina; 2001.
33. Tufail M, Hussain S, Malik F, Mirza T, Parveen G, Shafaat S. Isolation and evaluation of antibacterial activity of bacteriocin produced by lactobacillus bulgaricus from yogurt. Afr J Microbial Res 2011;5:3842-7.
34. Sah BNP. Identification of bioactive peptides produced by symbiotic yogurt having anti-cancer properties. A thesis submitted for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.
35. Kvit K, Kharchenko V. Role of gut microbiota in lipid metabolism. Asian J Pharm Clin Res 2018;11:1-4-8.
36. Pique N, Berlanga M, Minana Galbis D. Health benefits of heat-killed (tyndallized) probiotics: an overview. Int J Mol Sci 2019;20:1-30.
37. Lew LC, Liong MT. Bioactives from probiotics for dermal health: functions and benefits. J Appl Microbiol 2013;114:1241-53.
38. Mohammad Saeed W. Characterisation of the potential of probiotics or their extracts as therapy for skin. A thesis submitted to the University of Manchester for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.
39. Gueniche A, Bastien P, Ovigne JM, Kermici M, Courchay G, Sciences; 2014.
40. Pique N, Berlanga M, Minana Galbis D. Health benefits of heat-killed (tyndallized) probiotics: an overview. Int J Mol Sci 2019;20:1-30.
41. Lew LC, Liong MT. Bioactives from probiotics for dermal health: functions and benefits. J Appl Microbiol 2013;114:1241-53.
42. Mohammad Saeed W. Characterisation of the potential of probiotics or their extracts as therapy for skin. A thesis submitted to the University of Manchester for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.
43. Gueniche A, Bastien P, Ovigne JM, Kermici M, Courchay G, Sciences; 2014.
44. Pique N, Berlanga M, Minana Galbis D. Health benefits of heat-killed (tyndallized) probiotics: an overview. Int J Mol Sci 2019;20:1-30.
45. Lew LC, Liong MT. Bioactives from probiotics for dermal health: functions and benefits. J Appl Microbiol 2013;114:1241-53.
46. Mohammad Saeed W. Characterisation of the potential of probiotics or their extracts as therapy for skin. A thesis submitted to the University of Manchester for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.
47. Gueniche A, Bastien P, Ovigne JM, Kermici M, Courchay G, Sciences; 2014.
48. Pique N, Berlanga M, Minana Galbis D. Health benefits of heat-killed (tyndallized) probiotics: an overview. Int J Mol Sci 2019;20:1-30.
49. Lew LC, Liong MT. Bioactives from probiotics for dermal health: functions and benefits. J Appl Microbiol 2013;114:1241-53.
50. Mohammad Saeed W. Characterisation of the potential of probiotics or their extracts as therapy for skin. A thesis submitted to the University of Manchester for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.
51. Gueniche A, Bastien P, Ovigne JM, Kermici M, Courchay G, Sciences; 2014.
52. Pique N, Berlanga M, Minana Galbis D. Health benefits of heat-killed (tyndallized) probiotics: an overview. Int J Mol Sci 2019;20:1-30.
53. Lew LC, Liong MT. Bioactives from probiotics for dermal health: functions and benefits. J Appl Microbiol 2013;114:1241-53.
54. Mohammad Saeed W. Characterisation of the potential of probiotics or their extracts as therapy for skin. A thesis submitted to the University of Manchester for the degree of doctor of philosophy in the Faculty of Medical and Human Sciences; 2014.