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Original Article

CHARACTERIZATION AND SCREENING PARAMETERS OF SPRAY FILM-FORMING SYSTEMS: A COMPREHENSIVE STUDY ON DOSAGE FORMS AND QUALITY INDICATORS

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ABSTRACT

Objective: The objective of this study is to present the main screening parameters for the development of Spray Film-Forming Systems (SFFSs) using the design space. The focus is on characterizing the different phase states of SFFSs during application and establishing appropriate methods for determining the range of parameters.

Methods: In this study, various methods were used to determine the range of SFFS parameters. These include contact angle determination, pH test, viscosity measurement, drying rate estimation, spray pattern determination, tensile strength test, and washability. The methods used were evaluated and found to be effective in assessing the quality parameters of liquid concentrates, aerosols, and films of commercially available SFFS samples.

Results: Three states (liquid, aerosol, and solid) of commercially available SPSFs were evaluated using the techniques mentioned above. The applicability of the techniques and variability was discussed in comparison with similar studies. The results showed that the mean pH ranged from 5.43±0.02 to 6.63±0.05, the bioadhesion of liquid concentrates was in a narrow range of 4.49±0.52, the highest index of dynamic viscosity was 0.33±0.04, values of the spray pattern ranged from 6.19±1.97 to 17.46±2.72 cm2, bioadhesion values of the films ranged from 3.87 to 4.06 N, average values of film formation time were in the range of 65.55±12.65) s. 3 of the 4 samples had resistance to skin cracking, the tensile load of the commercial SFFS films varied from 2.91±0.3 to 5.11±0.65 N, and the tensile strength from 1.07±0.11 to 1.20±0.3 mPa. All films were not washed off with water.

Conclusion: The findings of this study demonstrate the successful application of tested methods in determining the range of parameters for SFFSs. The established values for indicators of liquid concentrates can serve as a basis for the further development of SFFSs. Overall, this research contributes to the understanding and standardization of Spray Film-Forming Systems for wounds, enabling their effective development and application in local skin treatments.

Keywords: Film-forming systems, Aerosols, Films, Liquid plaster, Bioadhesion, Spray pattern, Medical adhesives, Wound healing, Delivery systems, *In situ* formation

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INTRODUCTION

Conventional pharmacotherapy of wounds and burns aims to provide analgesia of the affected area, antiseptic action, removal of inflammation, and acceleration of cell proliferation [1, 2]. At the same time, many practitioners note that in most cases with an uncomplicated recovery process, it is enough to carry out primary treatment and isolation of the wound surface to prevent contamination and additional damage to the open area [3, 4].

Currently, liquid, semi-solid, and solid dosage forms are used in wound therapy. They can be applied either separately (sponges, plasters, films) or together with sterile dressing material (ointments, creams, gels, liniments, and aqueous and non-aqueous solutions). However, in some cases, the patient's self-treatment of the wound surface is complicated by the need for a sterile bandage and making aseptic conditions for its application. In such cases, it is possible to use spray film–forming systems (SFFSs) which are delivery systems for the local coating of the wound surface with an elastic polymer film formed *in situ*, which does not restrict movement. No need for direct patient contact with the wound surface (SFFSs are sprayed at a distance) repeatedly reduces the risks of additional mechanical damage to the wound and its contamination [5]. If patches or adhesive plasters are used, when they are removed or replaced, the affected area is traumatized [6]. SFFSs, unlike such dosage forms, can be removed without injury, especially when it is based on an aqueous film-forming solution [7]. In some cases, it can be washed off with a directed current of water to wash the wound.

The properties of the films formed *in situ* via SFFSs application can be varied to achieve the best wound healing. The films formed can be transparent (making it easy for the physician and patient to observe the wound), biodegradable, and water-washable. The variable occlusiveness of the films provides the necessary gas exchange for the wound and sufficient, but not excessive, moisture retention (water vapour transmission rate) and microbial protection [8]. The elasticity of the film protects the healing wound from opening and injury during movement.

The main advantage of films is that in the composition it is possible to achieve the antibacterial or antiseptic effect, as well as increase the wound-healing potential of the system by using the active components, for example, nanocarriers, growth factors, etc [9-12].

SFFSs are applied using a mechanical pumping system (spray-FFS) or a valve aerosol system (aerosol-FFS), which avoids the risk of cross-contamination of the wound and the medication, ensuring convenient application. It also allows local application control by varying the spray plume and using different spray nozzles [2, 5, 10].

SFFSs standardization should be carried out both before and after phase transitions, which are characteristic of all *in situ* systems. The authors of the different studies describing the development of SFFSs identify mandatory (included in the specification) and additional (screening or determined during development) standardization parameters [5, 9, 10, 13-16]. To find the optimal characteristics of the SFFSs and their values, the following characteristics can be distinguished: for film-forming concentrate: drying rate, pH, viscosity, stability and uniformity, contact angle, flour adhesion, for a spray system: the nature spraying (or spray pattern), for the formed film: thickness, elasticity, strength, visual uniformity, integrity, and also mucoadhesive characteristics-for the film. Additional indicators of films include washability or water resistance and occlusion [10, 13].

For 2023, in the global pharmaceutical market, SFFSs for use on wound surfaces are presented in the form of medical and cosmetic products containing or not containing active pharmaceutical ingredients. Meanwhile, the transdermal SFFSs on the market do not tend to meet the quality parameters that are rationally administered for medicines used on wounded surfaces.

The expansion of the range of SFFSs and the development of new medicinal products in this form is hampered by the lack of a generally accepted list of screening parameters, reproducible methods for their determination, and ranges of values that enable the production of SFFSs with the best biopharmaceutical properties [7].

The study aimed to study commercially available spray film-forming systems for wound healing to determine the ranges of their properties and capable methods of their determination for further use of the data obtained in the development of new dosage forms.

MATERIALS AND METHODS

The objects of the study were commercially available in the Russian Federation in the form of SFFSs (table 1). All samples were aerosols in cans of different volumes and with different valves.

Table 1: Name and manufacturer of SFFS-the object of research

Characteristics of SFFSs name of the SFFS, volume	Manufacturer	Category	Application of the SFFS	The composition as declared by the manufacturer
"OpsiteSpray", 100 ml	Smith and Nephew Ltd, UK	Medical device	Healing of clean, dry, surgical, or superficial wounds	Propylene–56%, Acetone/ethyl acetate–40.4%, Acrylic copolymer–3.6%
"LUXPLAST", 40 ml	Bolear LLC, Italy	Medical device	Protecting the wound from moisture and bacteria	Ethyl Acetate, Dimethyl ether, Ethyl alcohol Butyl Ether copolymer PVM/MA, Acetone, PEG-8, Olet-3, Stearalconium Chloride (concentrations were not provided)
"Afaplast with panthenol", 60 ml	Argo-Farm, Russia	Perfumery and cosmetic products in aerosol packaging	Wound protection from pathogenic microorganisms	Polymers, Isopropanol, Solvent mixture, Panthenol, Propellant (concentrations and types of propellant were not provided)
"Second skin PHARM Liquid patch", 150 ml	Green Life, Russia	Veterinary product	Treatment of skin lesions of various etiologies	Film-forming agent, Excipients, Dye, Butan-Propane, (concentrations were not provided)

According to sources pubmed. com the most selective, typical for SFFSs, reproducible methods for determining various indicators were selected, including the characteristics of both the concentrates (contact angle, bioadhesion, pH, dynamic viscosity), the spray system (drying time (film formation), spray pattern), and the film formed *in situ* (bioadhesion, tensile strength, cracking resistance). The rationale for studying a particular parameter was the possibility of its quantitative objective assessment, to use the results obtained in the future in determining the quality indicators of the SFFSs [7].

To determine the *contact angle* of the liquid SFFSs concentrate, a sample was applied to a glass plate and then the results were photofixed on a camera (FUJIFILM XT4, Japan) using a macro lens (FUJINON XF60 mm F2.4 R Macro, Japan). The results were studied and approximated in the Digimizer application (MedCalc Software Ltd, Belgium).

The pH of SFFS liquid concentrates was determined by the pharmacopeia method, according to the method described in USP<791>, using the laboratory pH meter Ohaus ST2100-E (Ohaus, Germany). Before each subsequent measurement, the electrode surface was carefully treated according to the instructions for use.

To determine the *dynamic viscosity* of film-forming compositions, it is possible to use various methods of viscometry. As an information value for understanding the subsequent spraying, simple cost-effective methods can be used to determine the dynamic viscosity. The technique involving the use of an Oswald viscometer has several limitations, primarily related to cleaning the device after the experiment.

The measurement of dynamic viscosity, based on Stokes' Law, was carried out using the "falling ball" method, the underlying operation of the Heppler viscometer. Traditionally, metal balls are used for such measurements, but for low-viscosity liquids, such as gel and film-forming solution in low concentrations, such balls are not suitable, since the speed of movement of the metal ball is often too high to accurately record the results of the experiment. As a replacement for a metal ball, a hydrogel ball made of sodium polyacrylate with a diameter of 10 mm was used in the study.

To determine the absorption of the solvent by the ball, its mass was previously measured on Analytical Balance ME54E scales (Mettler Toledo, USA). The ball was then kept in purified water for 5 min before being weighed again. The mass of the ball changed by ~ 0.015 g, a value that can be neglected, given that the time of passage of the ball through the solution was less than 3 min.

Two marks were fixed on a 10 ml measuring cylinder: start (8 ml) and finish (4 ml), the distance between which was 320 mm. The liquid FFS concentrate was extracted from an aerosol can, placed in a cylinder, and left for 30 min to remove air bubbles. The ball was placed on the surface of the concentrate and the time was measured by passing from the start mark to the finish mark (fig. 1).

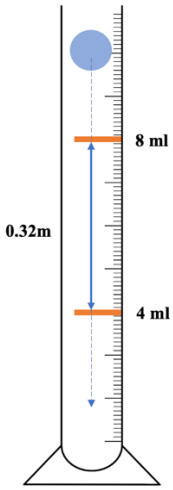

Fig. 1: Measurement of the dynamic viscosity of SFFSs liquid concentrates using the 'falling ball' method (Heppler viscometer)

The calculation of the results was carried out according to the formula:

$$\eta = \frac{2}{9} \times \frac{(\rho_l - \rho)R^2 gt}{l}, \text{ where}$$

η–the viscosity coefficient of the liquid,

l–the distance between the start line and the finish line, m,

ρ–ball density, kg/m^3,

ρ_l–liquid density, kg/m^3,

R–the radius of the ball, m,

g–acceleration of gravity, 9.81 m/s^2

t-time the ball moves from the start line to the finish line, s.

$$V_b = \frac{4}{3} \times 3{,}14 \times R^2, \text{ where}$$

V_b–ball volume, m^3,

R–the radius of the ball, m.

$$\rho_b = \frac{m_b}{V_b}, \text{ where}$$

ρ_b–ball density, kg/m^3,

m_b–ball weight, kg,

V_b–ball volume, m^3,

$$\rho_c = \frac{m_c}{V_c}, \text{ where}$$

ρ_c–concentrate density, kg/m^3,

m_c–weight of 1 ml of concentrate, kg,

V_c–volume of concentrate, m^3.

The literature describes many methods used to study *bioadhesion* on wounds and skin. They can be classified into two main groups: *in vitro/ex vivo* (for instance, using glasses, titanium, polyethylene, agar, mucosa, mucin, etc.) and *in vivo* (using the wound surface of a living organism) [17-19]. In this study, we used the method of measuring the separation force [20, 21], as one of the most popular, standardized, and easy to perform without the use of specialized texture analyzers.

In the experiment, a device (fig. 2) with a lever mechanism (fig. 2.1) was used to the moving (fig. 2.2) and stationary (fig. 2.3) parts of which SpanBond (Russia) nonwoven material was attached. A 20% (w/w) solution of porcine gastric mucin-type II (Sigma-Aldrich, USA) was applied to the lower part (fixed, fig. 3.3) and a test specimen (approximately 2x2 cm) was applied to the upper part. To the opposite pan (fig. 2.4) a load was placed and a critical mass was recorded at which the upper plate opens from the lower one. The results were processed according to the formula:

F = m × g, where

F–tensile strength

m–load weigh, kg;

g–Gravitational acceleration, 9.81 m/s^2.

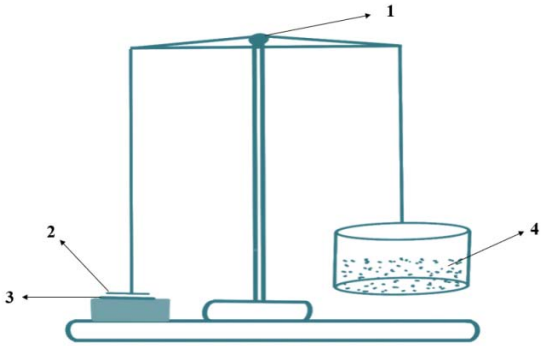

Fig. 2: A device for determining bioadhesion

The drying rate of the film was measured in standard conditions for all samples when applied to a glass plate (single spraying at an angle of 90°, focal length 100 mm), thermostatically controlled at 32±2 °C on the heating panel IKA C-MAG HS 7 digital (IKA, Germany). When the texture changes visually and the film dries, a 0.2 x 0.2 cm portion of the surface is swabbed with a cotton swab: if no fibres remain, the solvent is considered to have evaporated. If fibres remained on the film, the swab test was repeated in multiples of 10 seconds until the SFFSs were completely dry [13]. For uniformity of spraying, an electronic stopwatch VA-SW01 attorney ("Shenzhen Go Hand International Trade Co. Ltd.", China) was used, and the experiment was repeated in 10 repetitions.

To determine the *spray pattern*, white paper with a density of 80 g/m^2 was used, on which the test samples were sprayed at a distance of 100 mm by pressing the valve once (fig. 4). After each spraying, the two points furthest apart were marked, then they were connected and the line between them was measured. The results were sequentially included in table 7.

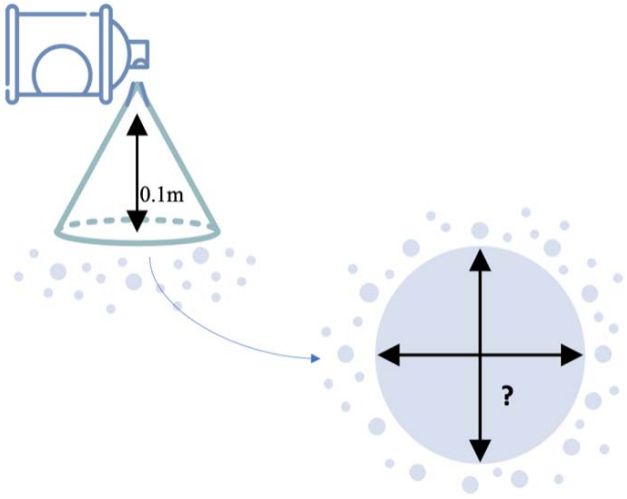

Fig. 3: Determination of the spray pattern

The tensile strength of the film was determined gravimetrically by the critical mass of the load leading to the tear. Films were prepared for the experiment. Each test sample with a volume of 20 ml was poured into Petri dishes, pretreated with glycerin, and left for several days until the films were completely dried in an oven sterilizer BINDER ED 23 Classic. The line at 30 °C. Then, the films were carefully separated from Petri dishes and cut into 20x50 mm samples.

The test of the obtained film samples was carried out according to the methods close to Sritharadol *et al.* (2017) studies [9].

The thickness of each film was measured in 5 places using a Harden micrometer (580832, accuracy 0.01 mm, measuring range 0-25 mm) to make sure that they were uniform. The arithmetic mean was determined if the thickness differed by more than 0.01 mm.

Calculations of the strength index were performed as follows:

$$\sigma = F \div Ao, \text{ where}$$

σ–tensile strength, mPa;

F-tensile load at the moment of breaking, N;

Ao–initial cross-section of the film.

The initial cross-section of the film was determined by the formula:

$$Ao = l \times b, \textit{where}$$

l–film thickness, mm, and b–film width, mm.

During the experiment, the mass of the load was gradually increased, and the critical mass was recorded when the film rupture was achieved. The tensile load was calculated using the formula:

$$F = m \times g, \text{ where}$$

m–mass, kg, g–gravitational acceleration, 9.81 m/s^2.

The results of the tensile strength measurement were compared with *the crack resistance.* The study was conducted on Nitrile Gloves (MedPride Powder-Free Nitrile Exam Gloves) filled with water (in preliminary tests, the distribution on the glove was similar to that on human skin). Samples were sprayed onto the glove, and after the solvent had evaporated, the glove was bent (up to 90°) and stretched slightly (~5 mm) to simulate the movement of the limb at the bending points. If the film cracked, it was considered unstable to crack (table 8).

Aluminum foil and cellophane film were checked as alternative materials and methods for investigating the film's resistance to cracking. The technique for both materials was similar: a substrate (foil or cellophane) was taken, the film was applied by brief spraying, and the film was completely dried (with a visual change in texture and drying of the film, a part of the surface of 0.2 x 0.2 cm was soaked with a cotton swab: if there were no fibers left, the solvent was considered evaporated), then the material was crumpled. If the film cracked, the film was considered unstable.

Statistical analysis

All experimental measurements were collected in at least triplicate. The data were expressed as the means±standard deviation (SD).

RESULTS AND DISCUSSION

Distinctive features of the SFFSs used. In the analysis of liquid concentrates of SFFSs, factors influencing the parameters determined in the future were noted. SFFSs "Afaplast with panthenol" is characterized by foaming when applied, which is not typical for other samples. The resulting film after spraying SFFSs is heterogeneous and has circular streaks, which, however, does not interfere with the determination of most indicators. However, air bubbles were present in the SFFSs "Second Skin PHARM Liquid Patch" after application and could not be removed until the film had solidified.

The authors of some recent papers on the development of SFFSs [5], point out that foam suppressants should be added to the compositions to avoid active foaming during spraying, which can affect the film's drying rate as well as its structural and mechanical properties.

The study of liquid concentrates of SFFSs

The contact angle was determined for SFFSs liquid concentrates in triplicate. The average contact angle of the "OpsiteSpray", "Afaplast with Panthenol", and "LUXPLAST" was determined to be 19±1°. For the "Second Skin PHARM Liquid Patch", the indicator could not be determined correctly due to the peculiarities of film formation, as noted above. Thus, the contact angle can be regarded as a variable parameter of SFFSs, as it can only be reliably determined for samples that form a smooth and homogeneous coating. The contact angle can differ due to both composition and surface properties. There are no standardized requirements for such a study of SFFSs. In the study of Sritharadol *et al.* (2017), the contact angle of the formulation was measured on a cellulose tubular membrane and ranged from 45.4±0.6 to 64.9±0.4 [9]. Thus, the results of the studies are difficult to compare when the formulations are aqueous or non-aqueous in different cases and different application surfaces are used. Accumulation of data from a pool of studies will be required for certain conclusions.

When studying the *pH* of liquid concentrates of the analyzed SFFS, a range of experimental average values from 5.5 to 6.5 was established (table 2), which partially meets the general requirements for dermatological preparations and agents applied to the wound surface. Normal skin pH is mildly acidic at pH 4-6, but the environment shifts with skin injury so that the pH values of the discharge from chronic wounds can be as high as 7.5-8.9 [22]. Local acidification of wounds favours the induction of fibroblast proliferation of epithelization and angiogenesis, limits bacterial colonization, and facilitates the release of oxygen from oxyhemoglobin [23, 24]. Thus, it can be assumed that the optimal pH values for preparations and medical devices applied to the wound surface should be about 6 and lower. The pH values are essential in the study of wound dosage forms [1, 9, 10].

Table 2: Results of determination of pH of liquid concentrates of SFFSs

Name of the SFFSs characteristics of SFFSs	"Opsite spray"	"Afaplast with panthenol"	"LUXPLAST"	"Second skin pharm liquid patch"
pH*	5.43±0.02	6.2±0.00	6.63±0.05	5.77±0.5

*Data are expressed as mean±SD, n=5

When studying *the bioadhesion of liquid concentrates* (table 3), it was shown that the adhesion value measured by the separation force from the surface treated with mucin for all liquid FFS concentrates is in a narrow range of 4.49±0.52.

Table 3: Averaged results of bioadhesion measurement of liquid concentrates and SFFS films

Characteristics and indicators name of the SFFSs	Form	Adhesion value, N*
"LUXPLAST"	Liquid concentrate	4.23±0.24
"Afaplast with panthenol"	Liquid concentrate	4.29±0.23
"OpsiteSpray"	Liquid concentrate	5.01±0.13
"Second skin pharm liquid patch"	Liquid concentrate	4.43±0.27

*Data are expressed as mean±SD, n=5

The *viscosity of the liquid concentrate* affects such indicators of the film formed *in situ* as film formation time, elasticity, strength, homogeneity, as well as the choice of a spray system for SFFS. Unlike mechanical spray pumps, aerosol valve systems are also capable of spraying viscous systems. There are modern (BOV) systems specially adapted for spraying viscous concentrates at any angle of the balloon, which may be relevant for new SFFSs being developed [25].

Among the medical and cosmetic SFFSs tested in this work, the highest index of dynamic viscosity is characterized by "OpsiteSpray" (0.33±0.04) (table 4). The dynamic viscosity of the remaining samples does not exceed 0.2 Pa· .s on average.

Viscosity can be used not only to establish a correlation between the spray characteristics of a particular system and polymer concentration during development but also as quality control in manufacturing.

Table 4: Results of measurement of dynamic viscosity of liquid concentrate SFFSs

Dynamic viscosity index name of the SFFSs	The weight of the ball is average, g*	The time of the ball falling, s*	Concentrate density, kg/m³	Dynamic viscosity, Pa · .s*
"Afaplast with panthenol"	0.54±0.02	1.74±0.13	980	0.14±0.11
"LUXPLAST patch-spray"	0.53±0.01	0.70±0.48	850	0.20±0.05
"OpsiteSpray"	0.58±0.01	0.65±0.06	820	0.33±0.01
"Second skin pharm liquid patch"	0.62±0.02	0.83±0.08	1100	0.13±0.04

*Data are expressed as mean±SD, n=5

The study of the aerosol form of the SFFSs

For aerosol systems, one of the important characteristics is the spray pattern. For SFFSs this characteristic is of particular importance since the volume of the dose extracted by a comparable valve opening time (1 sec), the diameter of the spot, and the area of the covered surface have a significant effect on the film formed *in situ*, its thickness, uniformity, tensile strength, cracking resistance, etc. [3, 4, 9].

Table 5: Determination of the SFFSs spray pattern

Name of the SFFSs characteristics of the spray pattern	"OpsiteSpray"	"Afaplast with panthenol"	"LUXPLAST"	"Second skin pharm liquid patch"
Diameter measurement, cm	4.7±0.37	3.83±0.13	4.6±4.3	2.77±0.48
Area measurement, cm²*	17.46±2.72	10.45±1.86	16.77±3.21	6.19±1.97

*Data are expressed as mean±SD, n=3

The results presented in table 5 indicate that the values of the spray pattern ranged from 6.19±1.97 to 17.46±2.72 cm². For the analyzed commercial SFFSs, the diameter of the spray pattern averaged from 2.77±0.48 to 4.7±0.37 cm.

Table 6: Averaged results of measurement of bioadhesion of SFFSs films

Characteristics of SFFSs name of the SFFSs	Adhesion value, N*
"LUXPLAST"	4.06±0.24
"Afaplast with panthenol"	4.05±0.52
"OpsiteSpray"	4.06±0.11
"Second Skin PHARM Liquid Patch"	3.87±0.09

*Data are expressed as mean±SD, n=5

Study of the characteristics of films obtained after spraying SFFSs

Along with the study of concentrate bioadhesion, it was of interest to determine the bioadhesion of the films, as the degree of adhesion of the films to the skin will influence the exposure of the active ingredients and the protective function of the film. The results shown in table 6 indicate that the bioadhesion values of the films are close and range from 3.87 to 4.06 N.

One of the most important screening parameters is the film formation time of the SFFSs. The results of determining the indicator for commercially available SFFSs are shown in table 7. The results correlate with other *ex vivo* studies of film adhesion. In a study by Pagano *et al.* (2020), the adhesion of wound-healing polymer films containing red onion was studied on porcine skin tissue (2 × 2 cm) using a dynamometer. The detachment force was 0.4 N±0.06, which is comparable to the results obtained in this study and described characteristics of the film [26].

Table 7: Determination of the film formation time of SFFSs (n = 5)

Name of the SFFSs	"OpsiteSpray"	"LUXPLAST"	"Afaplast with panthenol"	"Second skin PHARM Liquid patch"
Film formation time, s*	65.8±5.56	60.4±7.5	54.2±7.16	80±7.69

*Data are expressed as mean±SD, n=5

The lowest value of the film formation time was shown by "Afaplast with Panthenol"-54.2±7.16, the values of the indicator of other FFS are close (in the range of 65.55±12.65) sec.

There were no significant effects of the dynamic viscosity index, density, and other parameters of the liquid concentrate determined experimentally on the drying rate of the film, as shown with the analyzed SFFSs (table 7).

The factors affecting the drying rate are the type of propellant and the excipients in the SFFSs.

Washability or water resistance of the film

The behavior of the film applied to the skin when it gets wet is significant for the patient. All films applied by spraying SFFS samples on the back of the hand of healthy volunteers, after drying, were not washed off with a stream of water for 2 min. The "Afaplast with panthenol" film changed its structure (became white and similar to rubber) upon contact with water, after which its removal was very problematic and required the use of ethyl alcohol in high concentrations (above 70%) or acetone, which led to excessive

removal of moisture from the skin. Meanwhile, all solid (finished) films after getting wet, the films became brittle and lost strength and elasticity. Insufficiently strong and elastic films during thinning and sweating during operation can be destroyed by friction with clothing, which will violate the mechanical protection of the wound from external influences and occlusion, will lead to the ingress of film particles into the wound. Water-resistant films are often brittle and inflexible. To avoid these properties, plasticizers or water-soluble film-forming agents can be added [16]. When non-aqueous formulations are applied to wounds, the rapid evaporation of the solvent often results in over-drying of the wound, which is similar in effect to dry dressings that adhere to an over-dried wound surface and cause trauma upon removal or detachment [27]. Some polymers, such as PEG-400, serve as emollients, preventing excessive moisture removal. Such polymers often also serve as plasticizers in film-forming sprays [28].

According to the test results, the average *tensile load* of commercially available SFFS films varied from 2.91±0.3 to 5.11±0.65 N, and *the tensile strength* from 1.07±0.11 to 1.20±0.3 mPa. The results are shown in table 8.

Table 8: Results for tensile strength and cracking resistance of SFFSs films

SFFS characteristics name of the SFFSs	Ao, mm²*	F, N*	σ, mPa*	Resistance to cracking on the skin**
"LUXPLAST"	2.73±0.16	2.91±0.3	1.07±0.11	Yes
"Afaplast with panthenol"	4.57±1.86	5.11±0.65	1.20±0.3	Yes
"OpsiteSpray"	3.87±1.33	4.02±1.17	1.15±0.58	Yes
"Second skin pharm liquid patch"	3.9±0.95	2.95±0.21	0.79±0.2	No

*Data are expressed as mean±SD, n=5, **n=5

As shown in table 8, the SFFS "Second Skin PHARM Liquid Patch" has unsatisfactory durability and low resistance to cracking on the skin. The remaining studied SFFSs samples ("LUXPLAST", "Afaplast with panthenol", "OpsiteSpray") had similar values of tensile strength (1.14±0.34) and were resistant to cracking on the skin. The results have shown that the "tensile strength" test can make it possible to find *in vitro* optimal characteristics for a film that corrects resistance to skin cracking; however, this hypothesis requires additional study. Meanwhile, the test with resistance to cracking on the skin was the most indicative among similar *in vitro* tests on foil and cellophane, which was also tested as part of the study. The results obtained were comparable to those obtained for similar films in other articles, although they were inferior due to their water-soluble composition and lack of plasticizers [29, 30]. Further studies are needed to clarify the correlation.

CONCLUSION

The analysis of scientific publications devoted to SFFSs allowed us to determine their advantages and areas of application in the creation of medicinal products. SFFSs are *in situ* systems, so the peculiarity of SFFSs is that they change their state depending on the stage of use: during storage, these are liquids, at the time of evacuation from the package-spray systems, at the place of application–films, the quality of which will be determined, among other factors, by the quality of concentrate and aerosols. Therefore, to obtain standard films, each phase state of the SFFSs must meet certain criteria. The experimental data obtained from studying the characteristics of commercially available SFFSs allowed us to form approaches to quality assessment at each stage of the application of this complex pharmaceutical formulation. The main indicators are drying speed, pH, viscosity, stability and homogeneity, contact angle, and bioadhesion–for a film-forming concentrate); spray pattern–for aerosols; tensile strength, homogeneity, integrity, and also bioadhesion characteristics–for a film. The obtained parameters, as well as the results of certain values defined in the experiment, can be further used in the construction of design space parameters during the development of new drugs in the form of SFFS.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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