Textile Performances of Some Biomaterials with Controlled Release of a Drug for Cutaneous Therapies

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The paper is focused on the aspects of moisture, air, water vapor and heat transfer from human body to the environment, in the case of a textile material (100 % cotton knitting fabric with interlock structure), on which a layer of hydrogel or cyclodextrin derivative (mono chloro tryazinil-β-cyclodextrin) has been deposited, or a multilayer arrangement was executed with chitosan (CS) and sodium alginate (Alg) layers, alternately deposited. On the textile surface, one of the following medicines: hydrocortisone acetate (HCr), tacrolimus (TAC) and honokiol (HNK) has been inserted. The active principles are used in coetaneous therapies. One evaluates the comfort elements concerning textile wearing in assembly garments, whose main role is to release a drug from a textile surface to dermis. Tests have been performed on thickness, thermal conductivity, water adsorption, air and vapor permitivity of a basic textile material after chemical treatments meant to insert the hydrogel and cyclodextrin derivative. One obtained a relationship and a general overview between chemical treatments and the textile answer to comfort requirements of a garment, which is a therapeutic support for coetaneous pathologies.

Keywords: comfort, thermal conductivity, air and vapor permitivity

A large part of medical textiles is supports consisting of fibrous polymers that have the possibility to release a drug to the skin under the action of a stimulus. Drug release is accomplished in a therapeutic manner, depending on a certain coetaneous affection. In this context, we have as stages before producing a pilot model: i) form the temporary drug deposit; ii) establish the therapeutic dose; iii) modeling the condition of drug release to dermis.

The vestimentary comfort parameters have an important role in connection with clinically registered dermatologic affections; thus, the dermatologist establishes for the patient the selection criteria of adequate clothing as a therapeutically included condition. Through his prescription, the doctor means the realization of the coetaneous comfort necessary for optimizing the sensorial response [1-4] as the result of topical administration of the drug [5-8].

From a technical point of view, the comfort implies a thermo-physiological side objectively assessed using measuring equipment, a sensorial side, and finally a physiological side, the last two being subjective in their nature.

The thermo-physiological component imposes that the garment assembly is able to transfer the heat and humidity produced by the body to the environmental medium; or else, it establishes a coefficient of thermal conductivity as a threshold starting from which the heat transfer is considered as adequate, and a coefficient of permeability to air, water vapors and carbon dioxide. It is not easy to scientifically argument the determination of the threshold values, even if the textile products are fibrous polymers assembled in a structure for which there is a transfer of heat, moisture and air between human body and the environment. There is a significant variability from the point of view of human subject, depending on geographical position, hydration level, the season for which the estimate is made (cold or warm), patient age, and skin *p*H. The skin *p*H is correlated with age (the children have the *p*H closest to the neutral one, but when they grow up, the *p*H becomes acid); in the specialty environment, the mean *p*H value is considered *p*H = 5.5 [5].

In the conditions of the present study, the esthetical function of the medical textile is less important, and it passes on the second plane, unlike the comfort, which is an important criterion. Yet, one cannot completely ignore the esthetic aspect, especially at clothing articles destined to women.

In order to provide the comfort of medical textiles, one must establish at first the components of the system: human body - textile product - surrounding medium. Microclimate plays an important part in the irritations at coetaneous level [9]. The values of microclimate parameters for which the patient fills comfortable are: temperature: 32±1°C, relative humidity 50±10%, air displacement velocity 0.25 ± 0.15 m/s [4].

The sensorial comfort shows the manner in which patient coetaneous sensors perceive a textile surface; generally, it concerns the sensation perceived by the person who wears it at the textile/dermis direct contact, and it is expressed by syntagma: soft, rough, tight, loose, suffocating, etc. The sensorial comfort is in close connection with tactile aspects of garment articles touch. This can be perceived differently, given the fact that the derma stimulus is in fact the brain response to the signals sent by tactile sensors. The more pleasant (soft) is the touch, the more adequate is the textile product with the destination for which it was designed [6]. The physiologic comfort due to wearing an adequate textile product is important, because by wearing the textile material the

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patient can improve its physical condition based on coetaneous stimuli, which he perceives. On the other side, the patient is aware that the textile material that he wears, together with the released drug, can solve his health deficiencies determined by the coetaneous affections, irrespective of his will.

The selection of the textile material is chiefly related with product destination. Once destination established, one establishes the general characteristics of the textile fabric [7, 8]. The first condition is that the textile fabric has the size adequate to the subject. Namely, the clothing assembly (pyjamas, blouse, stockings, and panties) must be fitted to the anthropological dimensions in terms of conformation peculiarities of each patient. On the other side, the coetaneous comfort is the skin sensorial [9] response to the absence of folds, buttons, zips, sewing zones, constrictions on anatomical portions, etc, situated on the inside of underlinen worn by the patient.

From the structural point of view, it is known that: i) due to the presence of scales as a exocuticle morphological aspect, the woolen textiles initiate a severe itchiness, therefore they are not to be used in straight contact with the skin; ii) the synthetic textiles determine human subject irritability, due to the absence of the possibility of perspiration sorption, and to the textile tendency to electrostatic charging; given their structural input of protein materials from natural silk and wool can initiate allergic reactions.

The present work is dedicated to highlighting the comfort aspects of medical textiles after having attached a release system for coetaneous pathologies drugs.

Experimental part

Materials and Methods

During the investigation we have used as textile support a 100% cotton interlock knitting fabric, with yarn count Nm = 60/1. The interlock structure is currently used to manufacture blouses, undershirt, pajamas, trousers, panties, which are underclothes articles. Table 1 presents the codes used for the experimental variants subjected to study.

In the study, we have evaluated the following textile characteristics: thickness, specific weight, thermal resistance, air and vapor permeability, and vapor dynamic sorption respectively.

Before the tests, the textile samples were conditioned for 48 h under standard conditions, namely 20 ± 2°C and 65 ± 2% relative humidity.

We have used the following drugs: hydrocortisone acetate for coetaneous eruption on allergic background, tacrolimus, a new generation pharmaco-dynamic product for psoriasis therapy, and honokiol, an extract of the tree *Magnolia Officinalis*, used to treat skin cancer, as well as a natural active principle with anti-infectious action [8, 9].

The formation of a temporary reservoir of active substance on the surface of 100% cotton knitting fabric for HCr and HNK [10-12] is accomplished by obtaining a cross-linked ionic hydrogel of CS with Na_2SO_4. TAC is deposed on the 100% cotton knitting fabric, on which one has added alternative CS and Alg layers, the TAC being deposed between them. The release is performed by the perspiration, which solves the water-soluble polymer layers, thus making the drug available for the dermis. Figures 1-4 illustrate the structures of the active principles and hydrogel used in the work. Details on the parameters and stages of biomaterial formation on the textile surface are to be published.

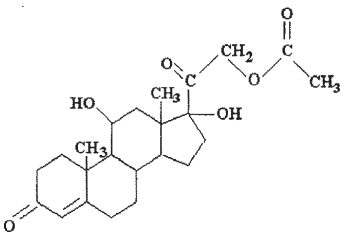

Fig.1. Structure of hydrocortisone acetate

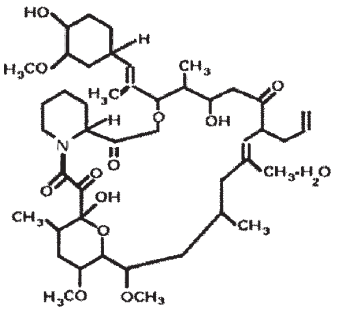

Fig. 2. Structure of tacrolimus

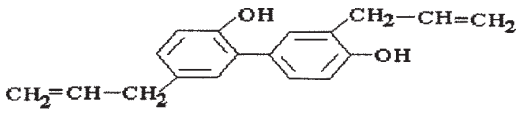

Fig.3. Structure of honokiol

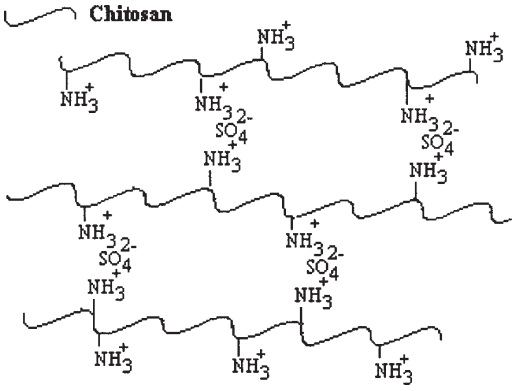

Fig. 4. Structure of CS based hydrogel and Na_2SO_4

Code	Sample abbreviation	Treatments on samples
1	Knitted witness	Alkaline boiling (AB) and bleaching with hydrogene peroxyde (BHP)
2	Knitted + MCT-β-CD	AB, BHP and grafted with MCT-β-CD
3	Knitted+ MCT-β-CD+ HCr	AB, BHP and grafted with MCT-β-CD and HCr complexed in CD
4	Knitted + CS	AB, BHP, with CS based hydrogel
5	Knitted+CS+HCr	AB, BHP, with with CS based hydrogel and HCr included
6	Tricot +CS+TAC	AB, BHP, with with CS based hydrogel and TAC included
7	Tricot+CS+HNK	AB, BHP, with with CS based hydrogel and HNK included

Table 1
CODES OF VARIANTS FOR COMFORT CHARACTERISTICS OF TEXTILE SAMPLES

Determination of the treated samples thickness

The tests were carried out according to the Standard SR EN ISO 5084:2001. For each knitting fabric sample (1÷5) sized 100 x 100 mm, five measurements were carried out (corners and center). Thickness evaluation is carried out with micrometer with disk; the micrometer measuring range is 0÷10 mm, with an accuracy of ±0.01 mm. The time of sample pressing was 30 s.

Determination of specific weight

In order to determine the specific weight (Ms) of a textile material, having as specific units (g/m^2), the experiments followed the standard procedure SR EN 12127:2003. The determination of the specific weight, i.e. of the textile sample mass on unit surface on small samples was carried out according to the standard SR EN ISO 139:2005.

At each experimental determination (1÷5), we needed 3 samples sized 100 x 100 mm, cut with an accuracy of 10^{-3}m, following the shape of standardized metallic pattern. The measurements were carried out both in the length direction and width direction. The weight g was obtained by weighting with electronic balance (ESJ 200-4 type) with an accuracy of 10^{-3}g.

In order to determine the specific weight of the knitting fabric samples, the following relation was used:

$$Ms = (m_m/Lm \cdot lm) \cdot 10^6 \ [g/m^2] \quad (1)$$

where m_m is the mean weight of the weighted samples; Lm and lm are mean dimensions of the samples measured after sampling from the piece of knitting fabric, in mm.

Water absorption determination

Determination of water absorption capacity is made according to STAS 12750-89 through total static immersion.

The knitting fabric samples (by three for each experimental variant) are square in shape, with the dimension of 100 x 100 mm and they are weighted after conditioning, before the experiment. The working protocol consists in the following operations: - samples immersion in water for 15 min.; - elimination of water excess by equal shaking on the direction of stitch wales and courses (10 times); water leaking from each sample for 120 seconds; - pressing between two sheets of filter paper; - sample weighting with ±1 mg accuracy.

The water adsorption capacity is determined with the following formula:

$$Cabs = ((M-M_0) / M_0) \times 100, \ \% \quad (2)$$

where: M_o is the initial sample mass (g), M, final sample mass after immersion in distilled water (g).

Vapour permeability

Permeability to water vapor represents the velocity of water vapor transfer through textile supports, being a permeation characteristic of a material. In this way, one evaluates the vapor flow from dermis through the textile material to the external medium. Vapour permeability is the characteristic property of materials to permit the passage of water vapors from mediums with high relative humidity, to lower humidity mediums.

Thermal resistance

Thermal resistance represents the material property to retain the heat within an inner space. The thermal resistance R is obtained from the relation (3):

$$R = \delta/\lambda \quad (3)$$

where: R is the thermal resistance equivalent to heat insulating capacity, having as measuring unit (m^2·Kelvin degree/w), δ is the textile material thickness (m) and λ is the coefficient of thermal conductivity, in (w/m·Kelvin degree). From the relation (3) it follows that the bigger is the textile material thickness, the higher is the thermal resistance and implicitly the higher is insulating capacity from the environment. One knows from specialized literature that cotton coefficient of thermal conductivity, λ= 0.07 w/ m· Kelvin degree.

Dynamic vapour sorption

The dynamic vapour sorption is a method used to determine the sorption-desorption isotherms for various textiles, in the present case for the knitting fabric used as basic support to produce biomaterials. The isotherms shape is closely related with the textile material dimensions and structure. Brunauer, Emmet and Teller (BET) developed a theory for multilayer sorption, having as a model the Langmuir theory. According to BET [13, 14], the Langmuir equation is applied to each adsorption layer. A molecule that meets an occupied active center from the absorbent surface does not leave this center immediately, forming for a short time period an adsorption complex. With the increase of vapor pressure, the number of free centers from the material surface diminishes, together with the number of the active centers occupied by nanoadsorbed molecules, because complexes of double or triple adsorption were formed. Multilayer adsorption of the vapors on a homogeneous surface implies the following equilibrium states:

$$\begin{aligned} &\text{Vapours + textile material support} \leftrightarrow \text{mono complex} \\ &\text{Vapours + mono-complex} \leftrightarrow \text{double complex} \\ &\text{Vapours + double complex} \leftrightarrow \text{triple complex} \end{aligned} \quad (4)$$

Permeability to vapours represents the capacity of some materials to permit the water vapors pass through them through the interstices, at the transfer from a medium with higher humidity to a medium with low humidity. This characteristic is a parameter that facilitates the skin physiology. Vapor permeability is correlated with the thermo-insulating properties of the textiles products [14].

The measurements for dynamic vapor sorption and sorption hysteresis were performed with an IGAsorp Dynamic Vapor Sorption apparatus with the following characteristics: minimum gas pressure 2 bar; resolution of 0.1μg for 100 mg, and sample containers made of stainless steel micron size mesh. Before sorption measurements, the samples were dried at 25°C in a flow of dry nitrogen (250 mL/min), until the weight of the sample was in equilibrium at a relative humidity (RH) less than 1%.

Results and discussions

Thickness determination

The table 2 presents the values of the thickness of witness knitting fabric samples, untreated and treated with active principles respectively (as averages of three values).

According to the obtained results, one can notice that the thickness value for the ungrafted witness sample (1) is bigger than for the sample grafted with cyclodextrin (2). An explanation of the thickness diminution could be the deformation (through tension and compression) of the structural surface of the knitting fabric due to padding,

Table 2
VALUES OF SOME COMFORT PARAMETERS

Sample	Thickness	Specific weight	Water sorption
	(10^{-3} m)	(g/m^2)	(g/m^2)
1	1.056	172.06	139.15
2	1.002	148.48	150.70
3	1.108	174.18	121.88
4	1.160	175.74	169.27
5	1.106	158.46	160.58
6	1.104	157.37	163.73
7	1.098	161.03	165.27

specific to grafting treatment. Another phenomenon occurs in the case of hydrogel formation. The hydrogel sample (4) has a bigger thickness due to the CS layer deposited on knitting fabric surface [15]. Yet, the knitting fabric sample with hydrogel and drug (5) shows a lower value of the thickness, because natrium sulphate used to CS cross-linking erodes the hydrogel layer.

Determination of specific weight

Table 2, column (3) presents the values of specific weight. What concerns the realization of an advanced comfort al coetaneous level, it is important that the textile support have a specific weight as small as possible. This means a diminished thermal resistance and therefore an adequate heat transfer from dermis through the interstices and knitting fabric stitches to the outside. According to the values from table 2, we can conclude that for the knitting fabric grafted with MCT-β-CD, the values of the specific weight (148.48 g/m^2) are smaller than for the ungrafted knitting fabric, because of structural modifications of the stitches, which are deformed through padding. For the knitting fabric grafted with CS-based hydrogel, the value of the specific weight is higher than for the witness knitting fabric, due to chitosan film existing on the fibrous surface. In the case of knitting samples grafted and treated with active principles, the specific weight is smaller, as compared to the ungrafted witness sample (specific mass = 172.06 g/m^2) as the integrity of the knitting stitches structure is affected by squeezing the knitting fabric during the padding operation. The variations of the specific mass do not have large values, such that the practical implications are not significant.

Determination of water absorption capacity

By determining the water absorption capacity according to STAS 12750-89 through total static immersion, one appreciates the water adsorption capacity of the knitting fabric and, implicitly, water permeability, being an index of textile material wettability.

The knitting samples (by three for each experimental variant) are square in shape, sized 100 x 100 mm; they are weighted after conditioning, prior to the experiment.

The experimental protocol consists in the following operations: - immerse the samples in water for 15 min; - remove the water excess by equal shaking both in the direction of stitch course and wale (10 times); - leak the water from each sample for 120 s; - press the sample between two sheets of filter paper; weight the samples with an accuracy of ± 1 mg.

Water adsorption capacity is determined with the following formula:

$$C_{abs} = (M - M_o)/M_o) \times 100, (\%) \quad (5)$$

where: M_o – mass of initial sample, (g); M- sample mass after immersion in water, (g).

Table 2 presents in column (4) the obtained values. The obtained differences have no practical relevance.

The textile materials behaviour related to water depends on the nature of the fibers they are made of, their structure and porosity, as well as on the intensity of preparation treatments applied to the material (alkaline boiling, bleaching with hydrogen peroxide, washing, etc).

The larger the water quantity absorbed by the material, the better is its absorption capacity and then the capacity to transport the perspiration from the skin to the material. Yet, the perspiration evacuation to the surrounding medium also imposes other conditions, which are detailed in the next chapters. Thus, the variants 4, 5 and 6, which imply the CS based hydrogel on the knitting fabric and have a significant swelling potential (a detail presented in another work to be published), having a porous structure, have maximal values as compared to the values in the cases where beta-CD is involved. In the case of variant 7, where HNK is used, it seems that the molecular volume and drug hydrophobia affects the humidity sorption by hydrogel, as compared to the variants 4, 5 and 6.

Vapour permeability

Water vapor permeability (PVA) of water vapors were evaluated on Permetest apparatus according to the Standard ISO 11092: 1993. (Determination of physiological properties, Measurements of thermal and water resistance under steady- state condition (sweating guarded hotplate)).

The measurements were carried out for triplicate (1÷7), in three distinct zones, giving finally the standard deviation and arithmetic average. The obtained values are presented in table 3. The values of water vapor permeability are higher for the knitting fabric grafted with CD, while the relative values were obtained for hydrogel. We do not know all the involved details, to explain the differences. Taking into account the obtained results and the data from literature, cotton materials present high water vapor permeability, which means an increased potential for vapor evaporation from the skin, and therefore a good capacity of perspiration transfer. This characteristic proves that cotton materials provide an adequate breathing capacity, as compared with the polyester materials, according to Yao and al. [16].

Thermal resistance

The thermal resistance (R) was evaluated on Permetest apparatus, according to the Standard ISO 11092:1993 (Determination of physiological properties, Measurements of thermal and water resistance under steady- state condition - sweating guarded hotplate).

Table 3 presents the values of water vapor permeability and thermal resistance of the samples with and without drug.

Table 3
DETERMINATION OF PERMEABILITY AND THERMAL RESISTANCE

Sample	P_{va} ± SD	R ± SD
	(Pa.m/W)	(m^2.grad K/W)
1	4.3±0.00	8.3±1.7
2	4.5±0.10	11.6±0.5
3	4.5±0.30	10.4±2.8
4	3.7±0.40	4.5±1.8
5	3.2±0.10	3.2±1.3
6	3.4±0.20	1.5±0.4
7	3.8±0.60	5.3±2.4

SD = standard deviation

Sample	BET		GAB		Weight (%)
	surface (m^2/g)	monolayer (g/g)	surface (m^2/g)	monolayer (g/g)	
Cotton knitted	178.19	0.0507	164.282	0.0467	8.8769
Knit +MCT-β-CD	176.436	0.0502	148.944	0.0424	10.0761
Knit + CS	197.516	0.0562	186.849	0.0532	10.3179

Table 4
COMPARATIVE RESULTS ON WATER ABSORPTION ON BIOMATERIAL SURFACE AND WITH CS-BASED HYDROGEL

What concerns the thermal resistance of textile materials, the higher its values, the smaller the heat loss [16, 17]. The values presented in this study indicate that the highest values of the thermal resistance are obtained for the knitting fabric grafted with CD. The smallest values of the thermal resistance are obtained for the knitting fabric grafted with hydrogel and active principles.

Dynamic adsorption of water vapors

Figure 5 illustrates the values of water vapor dynamic sorption obtained based on BET isotherm.

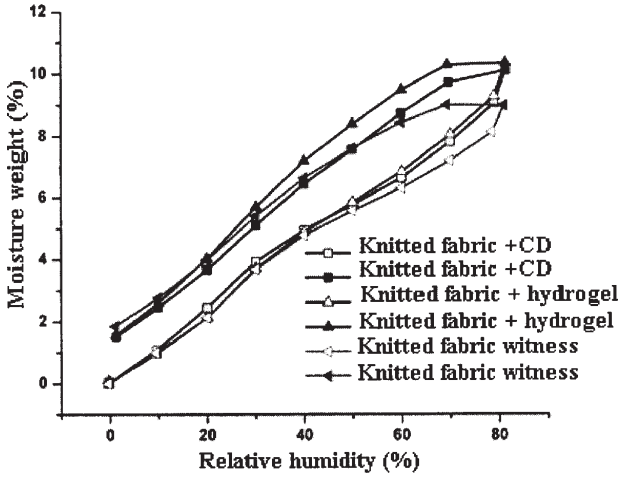

Fig. 5. Adsorption-desorption isotherm specific to cotton knitted fabric, knitted with CD and CS-based hydrogel

From figure 5 it follows that the biggest values of the adsorbed water are obtained for the knitting fabric with hydrogel, both in the part of sorption from small and big values of relative humidity, and in the desorption part. The explanation is that to the active centers of water centers from the knitting structure, determined by material porosity and the ability of hydroxyl groups to form hydrogen bonds with atmospheric water, one adds the active centers of water sorption specific to hydrogel (porous structure of carbohydrate). At large humidity, even the material with CS grafted on cellulose attaches a larger water amount than the unmodified cotton. The explanation consists in the fact that the CD cavities are hydrophilic at the outside. Thus, we give in figure 5 a comparison of three textile supports: a witness one of 100% cotton, the same material grafted with CD, and respectively with CS, which manifest numerous active centers due to hydroxyl groups from the corresponding carbohydrates, as well as to porosity, being typical hydrophilic entities. According with measurements performed are obtained moisture absorption and desorption isotherms of water on the biomaterial surface. In equation (5) is illustrated BET formula:

$$W = \frac{W_m C \cdot RH}{(1-RH)\cdot(1-RH+C\cdot RH)} \quad (5)$$

where: W_m = the ammount of monomolecular layer of water; RH=water activity; C = free absorption parameter.

Starting from above equation (5) one determined the GAB equation (Guggenhein, Anderson and der Boer), which represents another recent model to determine the absorption isotherms. BET equation equation is similar to GAB except that it uses in addition, an empirical constant K [18-20]. When K = 1, GAB equation becomes BET equation. Using two experimental equations aims to achieve an optimum experimental. The GAB equation covers a broader experimental modeling moisture sorption processes for most situations disclosed. Table 4 summarizes the experimental results obtained on the amount of water absorbed by the three types of samples from a monolayer of water molecules using BET and GAB equations.

According to the above results, the samples with CS and hydrogel have the highest ammount of water for both BET and GAB model; This is due to the porous structure and the existing OH groups capable of binding water by hydrogen bonds. In both cases, the amount of water attached to the surface of the two biomaterials (CD and knit fabric with hydrogel) reaches 10% compared with the control fabric which has a lower value (8.87%). In terms of garment comfort the biomaterial improves compared with the witness samples.

As a general characteristic of comfort determination, we can point out the obtained differences between the values of the characterizing parameters.

Conclusions

The biomaterials obtained by grafting the cyclodextrin derivative to cotton cellulose from the interlock knitting fabric manifest adequate properties of water sorption, good water vapor permeability and a thermal resistance specific to cotton articles with interlock structure. The hysteresis of dynamic water sorption-desorption characteristic shows an intermediate value between the textile support and the textile support with CS-based hydrogel.

The cotton-made biomaterials wit CS-based hydrogel have high values of water sorption, but gel presence is favorable to a maximum sorption, while drug inclusion in hydrogel determines a diminution of water sorption. From the standpoint of the dynamic sorption, in this case, the highest values are obtained as the result of the increased number of water sorption centers due to the porous and hydrophilic structure of hydrogel and cotton; the two manifest an additive character.

Drug application in the biomaterials has no significant influence on the comfort properties of the performed biomaterials.

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