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Effectiveness of citrus hystrix extract gel compress towards the lowering of body temperature on hyperthermia patients

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ABSTRACT

Background

Fever is a major complaint of various diseases in various ages. Hydrogel compress is a method of managing nonpharmacological fever of external hydrotherapy. Citrus hystrix has antipyretic phytochemicals. Therefore, compressing the gel with citrus hystrix extract is expected to reduce body temperature.

Objective

This research aims to determine the effectiveness of citrus hystrix extract gel compress towards the lowering of body temperature on hyperthermia patients in Dr. R. Soeprapto Regional Public Hospital in Cepu.

Methods

This research is a true experimental uses a research design pre test and post test control group design. Data collection involved 42 respondents of typhoid fever and DHF medical diagnosis, selected through techniques non-probability sampling with method stratified random sampling which is divided into 3 groups. Giving citrus hystrix extract gel compress 50% was given in the first treatment group, citrus hystrix extract gel compress 75% in the second treatment group and the control group was given a commercial hydrogel compress.

Results

Test results Mixed Between-Within Subject ANOVA showed a significant difference with p value 0.000 ($p < 0.05$) means that the treatment group is better at lowering body temperature than the control group, especially the treatment group with citrus hystrix extract gel compress of 75%.

Conclusion

Giving citrus hystrix extract gel compress for 60 minutes with 7 measurements every 10 minutes is very effective in reducing body temperature on hyperthermia patients diagnosed with typhoid fever and DHF.

Keywords: Compress, Extract Gel, Citrus Hystrix, Body Temperature, Hyperthermia.

INTRODUCTION

Hyperthermia is a common problem that becomes the main complaint of various diseases in various ages, ranging from infants, children, adults to the elderly. According to the Indonesian Pediatric Society hyperthermia is the most common reason for consultation and reaches 30% of total visits [1]. Besides the incidence of hyperthermia 2-5% in children aged 6 months - 5 years and there are 3-4% occur in adults [2]. Based on the results of the health service profile of West Kalimantan Province shows that throughout the year in Pontianak in 2016 there were 2394 cases manifested hyperthermia in children aged 5-14 years [3]. Next, the incidence of hyperthermia at the Ibnu Sina Regional Hospital in Gresik district for a period of six months from January to July 2017 showed a total of 776 patients [4]. From the results of preliminary studies in Dr. Soeprapto Cepu, hyperthermia is among the top 10 diagnoses and ranks first, counted from July to August 2019 as many as 125 patients, with an average of 40 patients per month [5].

Hyperthermia with temperatures $>38^{\circ}\text{C}$ can be dangerous, negative effects of hyperthermia that can be dangerous include dehydration, impaired electrolyte balance, lack of oxygen, neurological damage, shock and seizures. Hyperthermia with temperatures reaching 41°C , where the temperature becomes higher causing the risk of severe illnesses such as bactericidal events, pathological hypertension or infection of the central nervous system until it can be fatal until it leads to death. To minimize the negative effects of hyperthermia, optimal hyperthermia management is needed. Management of hyperthermia can be done by pharmacological and nonpharmacological measures [6].

Non-pharmacological actions to overcome hyperthermia include the administration of compresses. Plaster compress is one method of managing hyperthermia by external hydrotherapy that can be done. Plaster compress therapy with hydrogel has the advantage of providing a comfortable feeling for sufferers, soft skin, practical and easy, time to decrease the temperature is relatively fast and safe to use with drugs. Hydrogel has a water content high enough so that it can reduce the temperature of hyperthermia through the mechanism of heat absorption from the body and transferring heat to water molecules, then lowering body temperature through evaporation. Hydrogel

preparations are perceived as solids which move heat faster than liquid through conduction and work by activating the posterior hypothalamus which is the center of heat production regulation [7, 8].

Citrus hystrix DC Is one of the diversity of flora in Indonesia. Citrus hystrix by the Indonesian people is used as a food flavoring and aroma therapy [9]. Research on citrus hystrix is still limited compared to the availability of citrus hystrix in abundant nature. According to previous studies by it was found that Citrus hystrix contains active compounds such as alkaloids, flavonoids, phenolics, terpenoids, tannins and saponins. Further research proves that the extract of ethyl acetate and chloroform of kaffir lime has a cytotoxicity effect on cervical cancer cells, neuroblastoma and breast cancer. In addition, citrus hystrix skin has antioxidant, antimicrobial, anti-inflammatory, free radical and antipyretic activity [10].

Some studies mention the phytochemical content in citrus hystrix which has been proven as an antipyretic. Like phenolic phytochemicals, flavonoids and saponins work as antipyretics by suppressing prostaglandin production resulting in vasodilation of blood vessels so that it can reduce skin temperature quickly so that heat can be channeled either through conduction or evaporation mechanisms [11]. In addition, the phytochemical content of flavonoids can inhibit cyclooxygenase or lipooksigenase which inhibits leukocyte accumulation so that it does not become anti-inflammatory. Anti-inflammatory mechanism in kaffir lime allegedly by inhibiting the release of serotonin and histamine to the site of inflammation and prostaglandin synthesis from arachidonic acid by reducing the work of cyclooxygenase (COX) [12].

Phytochemical content of terpenoids in citrus hystrix extract skin can increase penetration in transdermal preparations, so that it will speed up the process of entering the phytochemical compounds of citrus hystrix that can work to lower body temperature. Besides terpenoids have a reversible effect on the stratum corneum of the skin, non-toxic with low irritation potential [13]. The results of other studies also prove that this citrus hystrix contains good antipyretics. Citrus hystrix extract has some significant antipyretic activity against albino rats without causing acute toxic effects. Based on these studies show that kaffir lime has potential as a

candidate for standardized herbal medicine (OHT) [14].

In research Rizady, et al (2016) with the title "The Effect of Onion (*Allium ascalonicum* L.) Compress Toward Body Temperature of Children with Bougenville Room Dr. Haryoto Lumajang Hospital " showed that shallot compresses could reduce body temperature in hyperthermia patients, with a mean temperature reduction in the intervention group -1.65°C while in the treatment group of -0.65°C , it was suspected that the onion phytochemicals in the form of flavonoids and allicin play a role in the process of reducing body temperature in hyperthermia patients [15]. A similar study by Seggaf, et al (2017) on "The Effect of Aloe Vera Compress on Body Temperature of Pre-School-Age Children with Hyperthermia in Siatan Hilir Public Health Center" shows that the use of aloe vera compress has an effect on decreasing body temperature in hyperthermia patients, with p value = 0.001 ($\alpha < 0.05$) with a temperature drop of 0.488°C [16].

Development of Dervish research on "Development of Polyvinyl Pyrrolidone-Based Hydrogel (PVP) Electron Beam Irradiation Results as Hyperthermia-Decreasing Plaster" shows that compressing with hydrogel preparations with various formulas can show a decrease in body temperature and decrease in time. Hydrogel formula I stated has the ability to reduce water temperature 40°C to 37°C faster than formulas II, III and IV, which is within 11 minutes. The hydrogel formula IV reduction time is 19 minutes. Commercial hydrogels take 12 minutes. While a decrease in temperature without hydrogel is achieved in about 37 minutes [17].

So far research on compresses with the use of citrus hystrix extract has never been studied, especially with the use of transdermal hydrogels as sedans to compress hyperthermia-lowering plasters is still rarely found.

Based on the description above, the researchers are interested in conducting research with the title "effectiveness of citrus hystrix extract gel compress towards the lowering of body temperature on hyperthermia patients" in the hope that the research results can be used as a reference in providing interventions for nursing diagnoses in increased

body temperature (hyperthermia) easily, precisely and effectively.

METHODS

This type of research uses true experimental research using pre test and post test control group design. This research arranged three groups: the first treatment group who were given 50% citrus hystrix extract compress gel, the second treatment group was given 75% citrus hystrix extract compress gel and the control group was given a commercial hydrogel compress without citrus hystrix extract 50% or 75%. The action of compressing citrus hystrix extract compress gel is given for 60 minutes with 7 measurements every 10 minutes in 1 intervention. Body temperature measurements can be done using a digital thermometer instrument and the results are recorded on the observation sheet. Body temperature measurements of respondents who experienced hyperthermia were done before (pre test) and after the intervention of these therapies (post test 1, post test 2, post test 3, post test 4, post test 5 and post test 6).

The population in this study were all patients who experienced an increase in body temperature undergoing treatment at dr. R. Soeprapto Regional Public Hospital in Cepu. Determination of a minimum number of samples using techniques non probability sampling with method stratified random sampling and based on inclusion and exclusion criteria as many as 42 respondents divided into three groups with 14 respondents in each treatment group (50% citrus hystrix extract compress gel therapy), 14 respondents in the second treatment group (75% citrus hystrix extract compress gel) and 14 respondents in the control group (commercial hydrogel compress therapy without 50% or 75% citrus hystrix extract compress gel).

In this study, researchers conducted data collection by means of observation, identification, interviews and filling in the observation sheets. The data collected was analyzed through the IBM SPSS program version 24.0, and continued with a different test that is parametric test (Paired t test and ANOVA Repeated Measure test). The processed data is used as a basis for discussing statement matters, which are then presented in table form so that conclusions can be drawn.

RESULTS

Table 1 Frequency distribution of respondents from age, gender, education, jobs and medical diagnosis based on demographic data

Characteristics	Treatment 50%		Treatment 75%		Control		P
	(n=14)		(n=14)		(n = 14)		
	n	%	N	%	n	%	
Age							
<= 20 Years	3	21.4	4	28.6	2	14.3	1.061
21-30 Years	2	14.3	2	14.3	4	28.6	
31-40 Years	5	35.7	4	35.7	7	50	
41-45 Years	4	28.6	4	28.6	1	7.1	
Gender							
Male	7	50	6	42.9	8	57.1	0.874
Female	7	50	8	57.1	6	42.9	
Total	14	100	14	100	14	100	
Jobs							
Farmer	3	21.4	1	7.1	1	7.1	0.363
Entrepreneur	2	14.3	1	7.1	4	28.6	
Housewives	2	14.3	5	35.7	4	28.6	
Traders	2	14.3	2	14.3	1	7.1	
Students	3	21.4	4	28.6	2	14.3	
College Students	2	14.3	1	7.1	2	14.3	
Total	14	100	14	100	14	100	
Education							
Elementary	6	42.9	7	7	6	42.9	0.596
Middle School	2	14.3	2	2	-	-	
High School	4	28.6	4	4	6	42.9	
Bachelor	2	14.3	1	1	2	14.3	
Total	14	100	14	14	16	100	
Medical Diagnosis							
DHF	7	50.0	7	50.0	7	75	1.000
Typhoid fever	7	50.0	7	50.0	7	25	
Total	14	100	14	100	14	100	

*Homogeneous Test

Based on the table above we get the data that the mean age, gender, education, jobs and medical diagnosis in the treatment group and control group

have the same significant p value >0.05 means the same or homogeneous.

Table 2 Description of mean and standard deviation of body temperature in the treatment group and control group at 7 times the of measurement

Body temperature	Group	n	Mean±SD	Min-Max
0 Minute (Time 1)	Treatment 50%	14	38.67±0.242	38.30-39.00
	Treatment 75%	14	38.57±0.315	38.00-39.00
	Control	14	38.67±0.242	38.30-39.00
10 Minute (Time 2)	Treatment 50%	14	38.55±0.213	38.20-38.80
	Treatment 75%	14	38.47±0.344	37.80-38.90
	Control	14	38.56±0.190	38.20-38.80
20 Minute (Time 3)	Treatment 50%	14	38.35±0.224	38.00-38.70

	Treatment 75%	14	38.21±0.354	37.60-38.90
	Control	14	38.42±0.172	38.20-38.70
30 Minute (Time 4)	Treatment 50%	14	38.17±0.251	37.80-38.50
	Treatment 75%	14	37.97±0.331	37.50-38.50
	Control	14	38.32±0.267	37.80-38.60
	Treatment 50%	14	38.00±0.251	37.50-38.40
40 Minute (Time 5)	Treatment 75%	14	37.74±0.290	37.40-38.40
	Control	14	38.18±0.262	37.80-38.60
50 Minute (Time 6)	Treatment 50%	14	37.75±0.265	37.30-38.20
	Treatment 75%	14	37.60±0.280	37.30-38.30
	Control	14	38.02±0.283	37.70-38.50
	Treatment 50%	14	37.61±0.259	37.20-38.00
60 Minute (Time 7)	Treatment 75%	14	37.49±0.302	37.10-38.00
	Control	14	37.77±0.423	37.10-38.60

**Descriptive Statistics*

From the table above shows that the average value of the body temperature of the treatment group decreased more than the control group with a mean value of 37.6°C - 37.49°C which is included in the

normal temperature category, while the control group is still in the category of body temperature exceeding normal limits.

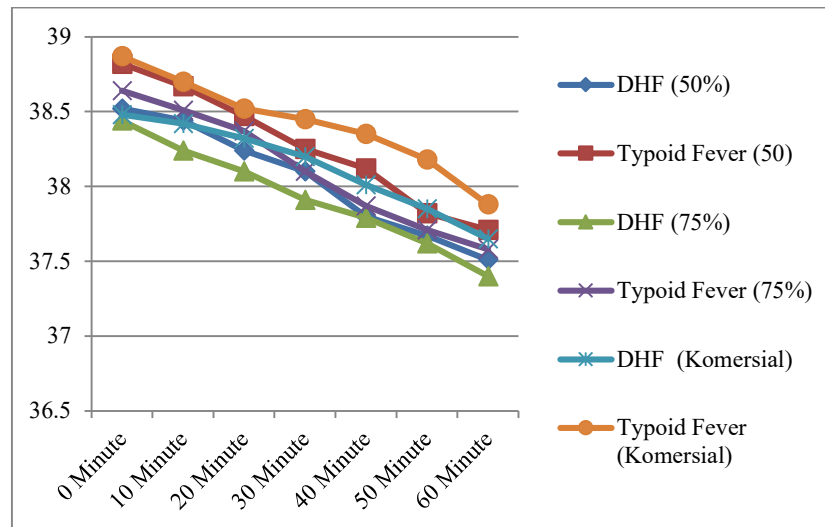
Table 3 Analysis of effectiveness citrus hystrix extract compress gel toward the body temperature in the treatment group and control group based on the type diagnosis

Variable		Treatment 50%	Treatment 75%	Control	P Value
Body Temperature	Type Diagnosis	Mean±SD	Mean±SD	Mean±SD	
0 Minute	DHF	38.52±0.205	38.44±0.340	34.48±0.134	0.000
	Typhoid	38.82±0.179	38.64±0.276	38.87±0.149	
10 Minute	DHF	38.44±0.207	38.24±0.369	38.87±0.125	0.000
	Typhoid	38.67±0.160	38.51±0.274	38.42±0.141	
20 Minute	DHF	38.24±0.222	38.01±0.330	38.32±0.112	0.000
	Typhoid	38.47±0.174	38.37±0.325	38.52±0.174	
30 Minute	DHF	38.10±0.274	37.91±0.330	38.20±0.223	0.000
	Typhoid	38.25±0.222	38.10±0.300	38.45±0.257	
40 Minute	DHF	37.80±0.213	37.79±0.211	38.01±0.167	0.000
	Typhoid	38.12±0.228	37.87±0.314	38.35±0.229	
50 Minute	DHF	37.67±0.221	37.62±0.195	37.85±0.113	0.000
	Typhoid	37.82±0.298	37.71±0.318	38.18±0.313	
60 Minute	DHF	37.51±0.219	37.40±0.350	37.65±0.222	0.000
	Typhoid	37.71±0.273	37.58±0.291	37.68±0.555	

**Repeated Anova Test*

Based on the table above shows that the minor hypothesis 1 is that there is an effect of differences in decrease in body temperature after the intervention in the control group and hypothesis 2 is

accepted that there is an effect of differences in decrease in body temperature after the intervention in the 50% treatment group and 75% treatment group.



Graph 1 Analysis of effectiveness citrus hystrix extract compress gel toward the body temperature in the treatment group and control group based on the type diagnosis

Based on graph 1 shows that the body temperature in both groups decreased according to the type of diagnosis of DHF and typhoid fever, but in the treatment group citrus hystrix extract

compress gel concentration of 75% showed more reduction in DHF than in the control group of 37.40°C.

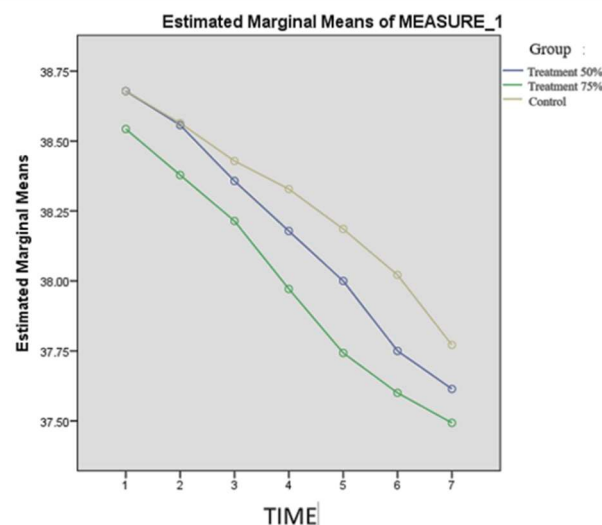
Table 4 Analysis of the mean difference in body temperature between the treatment group and control group

	Type III Sum of Squares	Df	Mean	F	P
Between Group	4,185	1	2,092	4.556	0.000

**Repeated Anova Test*

Based on the table above that there are significant body temperature differences between groups with a value of $F = 4.556$ and $p = 0.000$ (<0.05) indicate the F value for the "Body Temperature Between Groups" statistically

significantly different, so it can be said that there are differences in body temperature values between the treatment group and control group. When seen from the mean value among the treatment groups 75% more decrease than 50% treatment.



Graph 2 Decrease in body temperature between the treatment group and control group

Based on graph 2 shows that the body temperature of the three groups equally decreased, but in the treatment group 75% showed a decrease more than the 50% treatment group and control group.

DISCUSSION

The results of this research after being given a hydrogel compress intervention were measured up to 60 minutes in 1 intervention in DHF and Typhoid Fever patients with proven effective in reducing body temperature in measurements on post test 1 to post test 6 with a value of $p = 0.000$. The results of this research also showed that the DHF group who reached normal body temperature in the 40th minute were 2 respondents, in the 50th minute were 2 respondents, and in the 60th minute were 5 respondents while for the Typhoid Fever group in the 60th minute were 2 respondents.

The results of this study after given the intervention of 50% extract of citrus hystrix extract gel were measured up to 60 minutes in 1 time intervention in DHF and Typhoid Fever patients with proven effective in reducing body temperature in measurements on post test 1 to post test 6 with a value of $p = 0.000$. The results of this study also showed that the DHF group that reached normal body temperature in the 40th minute were 1 respondent, in the 50th minute were 2 respondents, and in the 60th minute were 4 respondents while for the Typhoid Fever group in the 50th minute were 1 respondent and in the 60th minute were 3 respondents.

The results of this study after the intervention of 75% extract of citrus hystrix extract gel was measured up to 60 minutes in 1 time intervention in DHF and Typhoid Fever patients with proven effective in reducing body temperature in measurements on post test 1 to post test 6 with a value of $p = 0.000$. The results of this study also showed that the DHF group who reached normal body temperature in the 40th minute were 3 respondents, in the 50th minute were 2 respondents, and in the 60th minute were 5 respondents while for the Typhoid Fever group in the 40th minute were 1 respondent, in the 50th minute were 2 respondents and in the 60th minute were 5 respondents.

This research shows that most of the hyperthermia is still above the normal temperature, most are in the Typhoid Fever group. The

characteristics of hyperthermia of these two diseases are indeed different. Typhoid Fever (TF) is hyperthermia due to *Salmonella Typhi* bacterial infection that spreads throughout the body. Symptoms of this disease develop for one to two weeks after a patient is infected by the bacteria. Common symptoms that occur in typhus include high body temperature reaching $39^{\circ}\text{C} - 40^{\circ}\text{C}$, headaches, muscle aches, abdominal pain, loss of appetite, fatigue and dirty tongue. Mean while, Dengue Hemorrhagic Fever (DHF) is a disease caused by the Dengue virus which is transmitted through the bite of the *Aedes Aegypti* mosquito. Early symptoms of DHF include high hyperthermia that lasts all day for 2-7 days over 38°C , manifestations of bleeding, platelets that go down continuously, hemoconcentration, enlarged liver, muscle aches, nausea and vomiting, and diarrhea [17].

Hyperthermia in DHF is caused by the production of various proinflammatory cytokines including interleukin-1 (IL-1), Interleukin-6 (IL-6) and TNF- α . Interleukin-2 (IL-2), interleukin 6 (IL-6) triggers prostaglandin production, affects the thermoregulation center, triggers complaints and symptoms of hyperthermia. Where as the typhoid fever virus is secreted by toxic substances by cells infected with the virus. Human typhi is very difficult in phagocytosis because it is protected by Vi capsule, only after some time the germ is in the patient's body there is a change in Vi capsule, so that the germ is now successfully phagocytosed by macrophages. At the stage of bacteremia, the destroyed bacteria will release endotoxins, which are lipopolysaccharide complexes which in turn activate the complement and stimulate the release of endogenous pyrogens from PMN cells, macrophages and other reticuloendothelial system cells. As well as removing Interleukin-1, which has a pyrogen effect. This endogenous pyrogen will affect the central temperature regulation in the hypothalamus and cause hyperthermia [17].

In this case hyperthermia in typhoid patients tends to be high because the germs are able to last longer and that is what will trigger bacteremia until the process of hyperthermia. So that the results of the study addressed the majority of the Typhoid group still in high temperatures after administration of the intervention.

The compress plaster is made of material hydrogel on polyacrylate-base with paraben content

formulated so that it can accelerate the process of heat transfer from the body to the compress plaster. Paraben is a white crystalline powder, which dissolves easily in methanol, ethanol and is difficult to dissolve in water which has antibacterial properties. The existence of a large water content in the structure of hydrogels can be used to reduce hyperthermia through the absorption of heat (energy) from the hyperthermia body parts and evaporation. Hydrogel is a polymer with a crosslink structure (crosslink) that contains large amounts of water (> 70%) [18].

This gel preparation is used as a carbomer 934 base because it has a high effectiveness in its role of providing good viscosity to the gel. At room temperature, carbomer can be stable for a long time and will remain stable or experience insignificant changes if there is the addition of antioxidant compounds in the formulation. Propelyglycol maintains the water content in the preparation so that the physical properties and stability of the preparation during storage can be maintained. Ethanol solvent is good to be used based on interest in the active compound.

The active substance from citrus hystrix in the form of saponin causes vasodilation of blood vessels will cause increased heat dissipation through the skin. Enlarged pores, heat expenditure by evaporation (sweating) is expected to be a decrease in body temperature to reach a normal state again. Phenolic and Flovanoid contain cyclooxygenase enzyme which suppresses prostaglandin biosynthesis, it is expected that body temperature can decrease. The content of terpenoids in kaffir lime skin can increase penetration in transdermal preparations that have a reversible effect on the stratum corneum of the skin, non-toxic with low irritation potential [19, 20].

Active substances of citrus hystrix extract in the form of saponins, phenolics, flovanoids, and terpenoids that have been released from the vehicle

(gel) will interact with the surface of the skin / stratum corneum. Active substances that have interacted with the stratum corneum will immediately diffuse into the stratum corneum. Diffusion that occurs is possible with the concentration gradient. Initially, diffusion of the active substance mainly takes place through the hair follicle (transfollicular pathway). After a steady state is reached, diffusion through the stratum corneum becomes more dominant. Diffusion of the active substance will eventually reach the deeper layers of the epidermis to the dermis. With the presence of blood vessels in the dermis, active substances from citrus hystrix with concentrations of 50% and 75% that reach the dermis layer will then be absorbed by the circulation system properly.

This is in line with that delivered by Nasrudin, drugs made from natural ingredients, such as herbs and other herbal products, are relatively safer to use. The product is relatively cheap and easy to get. Until now, infectious diseases including DHF and Typhoid Fever which can not be treated as a causal therapy with chemical drugs. There are several medicinal plants that have antioxidant, analgesic, antipyretic, antibiotic, anti-inflammatory, antiseptic properties and so on.

CONCLUSION

Based on the data processing and analysis regarding the administration of compress citrus hystrix extract compress gel, it can be concluded that the average reduction in body temperature in the treatment group compressed citrus hystrix extract compress gel 75% with a difference of 1.08°C more than the average a decrease in body temperature in the treatment group compressed citrus hystrix extract gel 50% with a difference of 1.06°C and a compress of commercial hydrogel with a difference of 0.90°C.

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