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Medicament testing on acupuncture points as a non-invasive diagnostic tool for determining the daily doses of sofosbuvir in patients with chronic hepatitis C virus infection

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Abstract

Background Acupuncture points are known for their unique bioelectric properties. Medication testing at acupuncture points has not previously been used to determine the daily doses of sofosbuvir in patients with chronic hepatitis C virus infection.

Results This pilot study included 61 patients with a confirmed diagnosis of chronic hepatitis C virus infection. Medicament testing of acupuncture points of the liver meridian ("Xing-jian") and Voll's circulation meridian ("Cells and lobules of the liver") was performed to determine the daily doses of sofosbuvir. A correlation analysis was carried out between the tested doses of the drug and the viral load in the blood of patients to confirm the results of testing the daily doses of sofosbuvir. Patients with chronic hepatitis C virus infection showed a significant positive correlation between tested daily doses of sofosbuvir and viral load in their blood. The mean values of the tested doses of sofosbuvir did not vary at different acupuncture points and significantly differed depending on viral load.

Conclusions This study showed that acupuncture points can serve as a diagnostic tool in the process of medicament testing and allow the determination of daily doses of sofosbuvir in patients with chronic hepatitis C virus infection. To further assess the clinical applications and physiological basis of medicament testing methods, additional clinical and instrumental studies are needed with a large sample of patients.

Keywords Electrodermal, Medicament testing, Daily doses, Electroacupuncture according to Voll, Skin resistance, Sofosbuvir, Hepatitis C virus

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Background

Acupuncture is a part of traditional Chinese medicine in which the impact on the body is made by special needles introduced at certain points on the human body, which are called acupuncture points (AP). Different properties of AP have been investigated, but the greatest interest is caused by their unique electrical characteristics [1, 2]. Numerous studies have shown that APs exhibit lower electrical skin resistance and higher capacitance than surrounding tissues, and various physiological dysfunctions affect skin electrical properties. The changed skin resistance of AP under the influence of various factors detected during electrodermal measurement might be significant for diagnostic and research purposes [3]. On the basis of the AP bioelectrical properties, various diagnostic devices for measuring electrical skin resistance have been developed, among which electroacupuncture according to Voll (EAV) deserves the most attention. Unlike other methods of acupuncture diagnostics, the EAV diagnostic uses a direct current of a subthreshold value and with a high internal resistance equal to 5.5–11.25 mA at a maximum voltage of 1.2 V (V), which interacts with the AP through the diagnostic probe of the EAV device [4].

Chronic hepatitis C virus infection (CHCV) is a major public health problem and can result in serious, even life-threatening, health problems such as cirrhosis and liver cancer [5]. Globally, an estimated 58 million people have chronic hepatitis C virus infection**,** with approximately 1.5 million new infections occurring per year [6]. Recent advances in the treatment of this disease with the use of pan genotypic direct-acting antivirals against hepatitis C virus have led to significant success, expressed in the complete or almost complete elimination of the virus from the patient's body [7]. Uzbekistan, one of the Central Asian countries, is among the states with a high prevalence of CHCV infection, which prompted us to start research on the use of medicament testing to determine the daily doses of the antiviral drug sofosbuvir, which belongs to the group of drugs recommended for the treatment of this disease [8]. The novelty of this study is that the task of studying the reaction of electrodermal measurement of acupuncture points to external influences in the form of indirect contact with an allopathic preparation has not been previously set. For the first time, an attempt was made to compare the results of the tested daily doses of the antiviral drug sofosbuvir obtained as a result of medicament testing (MT) and the level of blood viral load in patients with CHCV infection.

Methods

Search strategy, inclusion, and exclusion criteria

This pilot study was conducted at the Out-Patients Department of the Institute of Virology (Uzbekistan) together with the Medical Center, where the individual daily doses of antiviral drug sofosbuvir (Sovaldi)—400 mg (Natco, India) were selected for the patients. The dates included were from 2011 to 2021. The selection of patients in the Out-Patients Department of the Institute of Virology was carried out by random sampling. The following were the inclusion criteria: subjects of either gender, aged 16 to 75; the diagnosis was based on guidelines of the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA,2013); and patients willing to sign the written informed consent form. Patients without signs of chronic liver failure and liver cirrhosis. The study was approved by the Ethics Committee of the Ministry of Health of Uzbekistan (No 08/2,16.02.2011).

Study procedures

At the baseline visit, 61 patients (35 males and 26 females, aged 19–74 y.o) with a confirmed diagnosis of chronic hepatitis C virus infection (HCV Ab, qualitative and quantitative HCV detection in Real-time PCR (Amplicor Monitor Test, v.2.0., "Roche Diagnostics") were enrolled in the study. All enrolled patients were assigned to a single group and were examined by the medicament testing method by two experts in medicament testing with 31 and 20 years of experience. The examination of patients, registration of complaints, and medical history were conducted with the participation of the physician in a general clinical setting of the Medical Centre. All patients signed written informed consent forms for the study. MT was performed with an apparatus for EAV diagnosis called "Vistron" (Kindling, GmbH Medizintechnik) equipped with the EAV Homopath^{R} S software system [9, 10]. MT and protocol were followed according to the manufacturer's standard. The readings of the tested AP were collected and analysed.

Medicament testing

Medicament testing (MT) is a non-invasive express-method based on the electrodermal measurement of AP that allows finding the causes of various pathologic processes in the patient's body (EAV Homopath^{R} S software system); it allows the selection of different medicines and their doses individually for each patient. The MT algorithm includes the following stages: first, the electrical skin impedance is measured in the desired AP, and its initial value is recorded according to the parameters of the EAV device. The EAV Homopath^{R} S software helps make preliminary aetiological diagnosis of the disease, as it contains information on nosodes, which are homoeopathic preparations consisting of potentiated antigens and their components of various

viruses, bacteria, fungi and other infectious agents [11]. Having determined the pathogen, the expert can:

- Use MT to clarify the reliability of causative agent identification by placing the allopathic drug into the external test honeycomb;
- Select the optimal drug for the patient's therapy and determine its dose. To this end, various drugs are used since for each pathogen, there is its own group of drugs, e.g. antibiotics for bacteria and antiviral drugs for viruses. For instance, depending on the virus taxonomy, certain antiviral medicines are introduced into the patient-device circuit. For hepatitis C, these are inhibitors of NS5A/NS5B polymerase and NS3/NS4A protease, namely sofosbuvir, daclatosvir, ledipasvir and others.

The EAV diagnostic device contains the core apparatus with an external test honeycomb (for MT), the point-probe, metallic hand electrodes and a computer equipped with a software system. During an EAV diagnostic, a patient holds the metallic hand electrode, which is connected by a wire to the EAV device. At the same time, an expert in Voll diagnosis completes the electrical circuit by pressing on the patient's AP of interest with the point probe. Acupuncture point measurements are displayed in analogue as a light bar on the light bar display. The measurement scale is divided into 0–100 units. Depending on the results obtained when performing an electrodermal measurement of AP, the interpretation of the results is as follows [12]:

- The electric current of the AP and the device are identical in terms of the interaction, which corresponds to 50–70 units of the device's display scale and indicates the so-called energy balance or healthy condition of the organ under examination.
- The electric current in the AP exceeds the current supplied by the device, and therefore, the readings will be more than 70 units of the device's display scale. It is interpreted as the presence of a hyperergic reaction that is associated with some pathology of the organ due to intoxication of the body by some inflammation, etc.
- The electric current AP is less than the supplied current of the device, and therefore, the readings of the device are less than 50 units of the device's display scale and are interpreted as hypoergic reactions, corresponding to the concept of energy deficiency and correlating with the concept of the emerging or formed chronic course of the disease.

The second feature involves recording the phenomenon of *the indicator drop* when, upon reaching the maximum values on the display of the device, a reverse movement of the device indicator towards zero is carried out. If the AP under examination showed an indicator drop, the drug was placed into the external test honeycomb. *Medicament testing* is based on and used to test different medicines: their individual selection, selection of their doses, compatibility of drugs, etc. Table 1 shows the different options for the indicator drop and interpretation of the obtained [13].

When a specific drug is placed into the honeycomb during MT, changes in the absolute value of the device readings are observed, and it should be considered that this drug will have some therapeutic effect on the organ (related to the AP under examination). Table 2 shows the evaluation of the MT results [14].

To determine the daily dose of sofosbuvir, the drug was placed into the honeycomb of the EAV device at the recommended daily dose of 400 mg according to the instructions. The skin resistance at the acupuncture point was measured before and after placement of the drug into the honeycomb. In the absence of a positive reaction of the indicator of the EAV apparatus to the tested dose of sofosbuvir, an additional tablet of the drug was added to the honeycomb one by one, and each time the skin resistance was measured at the AP. The number of tablets at which a positive response was observed when measuring skin resistance at the acupuncture point was considered the detected daily dose of the drug [15].

Table 1 Interpretation of the results of the indicator drop (pressure on the acupuncture point with point probe less than 5 s)

Magnitude of Indicator Drop (CU)	Interpretations
Less than 2CU	Permissible measurement error (not taken into account)
Up to 5CU	It is interpreted as a slowly progressive destructive process with a compensated violation of tissue and energy condition
From 5 to 10CU	It is interpreted as a slowly progressive destructive process in tissues with compensated metabolism of matter and energy
From 11 to 25CU	It is interpreted as progressive degeneration of tissue and cellular structures with pronounced destructive processes (decompensation process)
25CU and over	Interpreted as an irreversible degenerative process with decompensated dysfunction (pronounced clinical picture of the disease)

Table 2 Assessment of medicament testing results

	Indicator readings after medicament placement into the honeycomb	Tested drug effect on the AP
1	No changes	No effect
2	The fall of the indicator is slowly dropping down	Positive impact
3	The indicator stops dropping	Positive impact
4	The indicator returns to normal values (50–64CU)	Positive impact
5	The indicator shows more significant dropping	Negative impact

To achieve our goal of research, we explored for diagnostic purposes both AP of classical Chinese acupuncture and AP proposed by Voll. Taking into account the extrahepatic replication of hepatitis C virus [16], we selected the following points of acupuncture for MT: 1. "Xing-jian" (LR2, the back-lateral surface of the proximal phalanx of the first toe at the place of transition of the head to the body, 1 mm depth). This corresponds to Voll's interpretation of this AP called "Cells and lobules of the liver" [17]. The second acupuncture point is located on the meridian of the pericardium according to the Chinese meridian system. In Voll's interpretation, it is called the circulation meridian, and the AP is called the "thoracic lymphatic duct," which is located on the palmar-radial surface of the 3rd metacarpal bone at the point of transition of the head into the body. Classical Chinese acupuncture does not indicate this AP, and it was proposed by Voll.

According to the MT data, the dose of sofosbuvir in the same patient at different acupuncture points varied in the quantity of medicine (the liver and circulation meridians). Because the study was conducted on acupuncture points of two different meridians, to analyse the data we obtained, the decision was made to use the maximum tested dose in one of the two tested acupuncture points in one patient. We concluded that the maximum tested doses of the medicine were comparable to the level of viral load in the patient's blood. A viral load allows us to detect the genetic information of the RNA virus in a blood sample and count its amount and is determined by HCV quantification by real-time PCR [18]. To analyse the obtained information, decoding of the viral load for hepatitis C (ME/ml) was used [19], which corresponds to:

Degree of severity	Viral load in ME/ml of blood
Low	600 to 30,000 copies/ml
Moderate	30,000 to 800,000 copies/ml
High	over 800,000 copies/ml

Statistical analysis

Descriptive and comparative statistics were used for statistical processing of the findings (Microsoft Excel 2010). Statistical analysis results were expressed as the mean ± standard deviation. To examine the strength of the association between the variables, a correlation analysis between viral load and tested doses of sofosbuvir in patients with chronic viral hepatitis C was performed. To determine the closeness of the relationship, we determined the coefficient of determination R.

Results

Comparing the results of the diagnosis of hepatitis C virus obtained by us in the process of MT with the results obtained by tests of traditional medicine, we obtained 96.7% data match ($P<0.001$). We used the following nosodes to diagnose hepatitis C virus: HCV virus and RNA polymerase, which are homoeopathic preparations of hepatitis C virus antigen and the enzyme responsible for virus replication in the human body [10]. The third marker of the disease was the drug sofosbuvir, which is an HCV NS5B nucleotide polymerase inhibitor. Due to doubts we had when comparing the obtained data with data on traditional medicine, two patients were excluded from the analyses.

In each tested AP, the readings of the device were recorded below the normal indicators of the electroacupuncture apparatus and were interpreted as a hypoergic reaction, which corresponds to the concept of energy deficiency. In both APs, the phenomenon of the indicator drop of varying severity was observed, the results of which were evaluated according to the accepted "Interpretation of the results of the indicator drop" (Table 1). Positive responses to the nosode of HCV virus, RNA-polymerase nosode and sofosbuvir by the MT method were registered in tested APs in 100% of diagnosed patients.

We analysed the relationship between viral load and tested doses of sofosbuvir in the general group of patients. Figure 1 shows the relationship between the tested doses of sofosbuvir and the viral load in patients with CHCV infection (Figs. 2, 3).

The presented diagram demonstrates a direct relationship between the tested dose of the SMV in the blood of patients.

To study the strength of the relationship between variables, we conducted a correlation analysis between viral load and tested doses of sofosbuvir in patients with CHCV infection. Additionally, to determine the closeness of the relationship, the coefficient of determination R was determined.

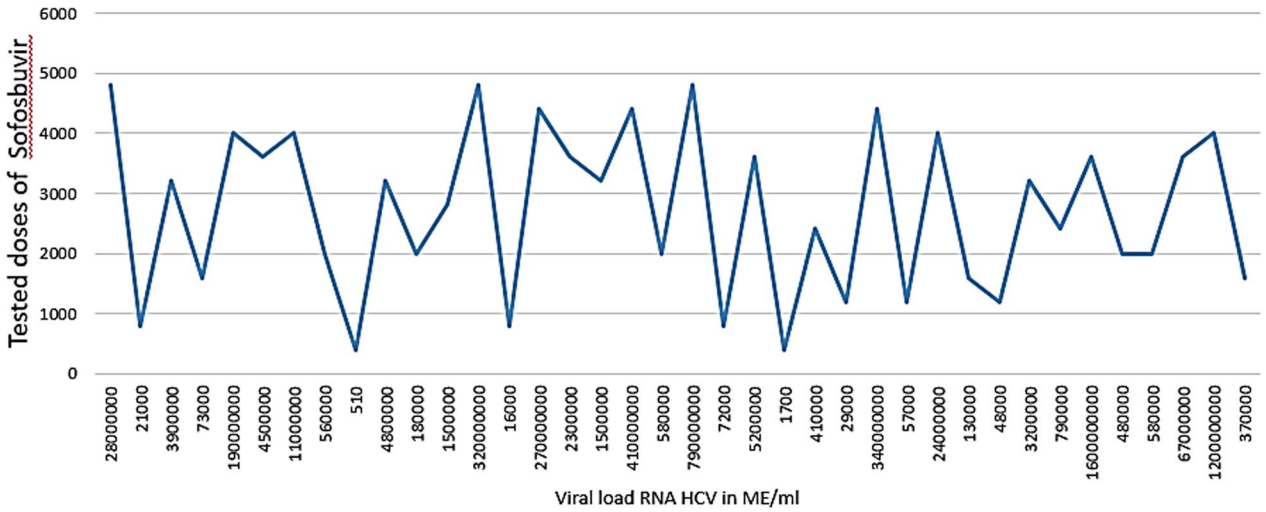

Fig. 1 Relationship between the tested doses of sofosbuvir (400 mg) and viral load in patients with CHCV infection

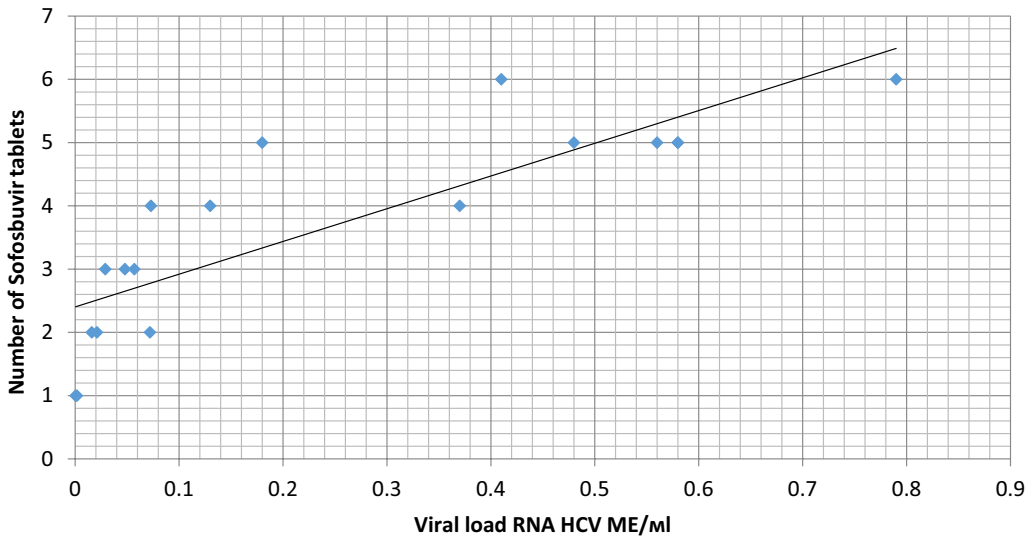

Fig. 2 Correlation between viral load and the number of tested tablets of sofosbuvir at low and moderate levels of viral load in patients with CHCV infection. ($r = 0.83$)

As seen from the figure, there is a direct correlation between the tested doses of sofosbuvir and the level of viral load in patients with low and moderate severity of viral load; the higher the tested dose of sofosbuvir, the higher the viral load in this group of patients.

To determine the closeness of the relationship, we determined the coefficient of correlation r. The data presented in Table 3 show that there is a strong correlation between the tested doses of sofosbuvir and the low and moderate levels of viral load in patients with CHCV infection. In this group of patients, the correlation coefficient was $r = 0.83$ on the Chaddock scale, which corresponds to a high (strong) positive correlation, whereas in the group of patients with a high viral load, the correlation became weak at $r = 0.27$, indicating that there was no association between the viral load dose and the tested dose of sofosbuvir. To understand the close relationship between the viral load and tested doses of sofosbuvir (400 mg), we calculated the coefficient of determination R (r^2), which was $R = 0.68$, meaning that in 68% of patients, the variability in tested doses of sofosbuvir was dependent on the viral load level. The coefficient of determination demonstrated that the variability in the number of tested tablets of sofosbuvir depended on the level of viral load (68% of patients) (Tables 4 and 5).

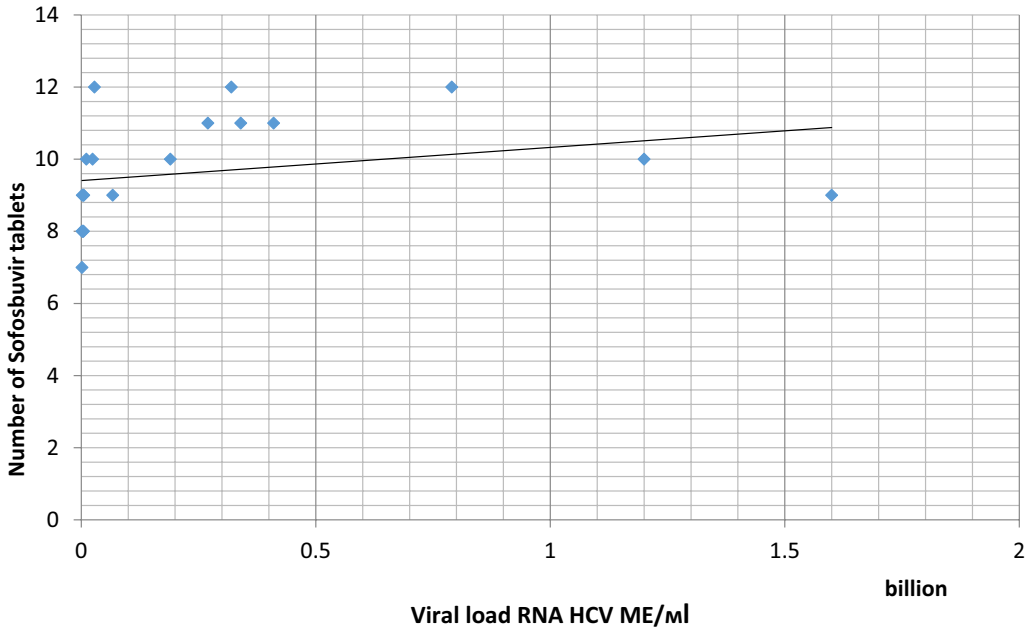

Fig. 3 Correlation between viral load and number of tested tablets of sofosbuvir in patients with high viral load in patients with CHCV infection ($r = 0.27$)

Table 3 Coefficient of correlation and determination between the amount of HCV RNA and tested doses of sofosbuvir with different levels of viral load

Correlation coefficient for low and moderate levels of viral load	Determination coefficient for low and moderate levels of viral load	Correlation coefficient for high level of viral load	Determination coefficient for high level of viral load
$r = 0.83$	$R = 0.68$	$r = 0.27$	$R = 0.07$

Table 4 Mean values of tested sofosbuvir tablets in patients with CHCV infection in different APs

Patients	Mean values of tested sofosbuvir tablets (M ± m)	Mean values of tested sofosbuvir tablets in the Liver meridian (M ± m)	Mean values of tested sofosbuvir tablets in the EAV Circulation meridian(M ± m)
(n-59)	6.8 ± 0.55	6.23 ± 0.56	5.15 ± 0.49

M ± m reflects the mean values of the measured values with an arithmetic mean error

In the group of patients with low and moderate viral loads, the correlation had a high positive correlation ($r = 0.83$). In this figure, we have presented the data for sofosbuvir in terms of the number of tablets tested.

Table 5 Mean values of tested sofosbuvir tablets in patients with different levels of viral load

The number of tested sofosbuvir tablets	The number of tested sofosbuvir tablets in patients with low and moderate level of viral load	The number of tested sofosbuvir tablets in patients with high level of viral load
6.8 ± 0.55	3.6 ± 0.537	9.65 ± 0.33

M ± m reflects the mean values of the measured values with an arithmetic mean error

In patients with a high viral load, the correlation became weak and amounted to $r = 0.27$, which indicates that there is no relationship between the viral load and the tested dose of sofosbuvir in this group of patients. In this figure, we have presented the data for sofosbuvir in terms of the number of tablets tested.

We found no significant values when comparing the mean values of tested tablets of sofosbuvir in patients with CHCV infection in different meridians.

When comparing the mean values of the tested sofosbuvir tablets in patients with CHCV infection depending on the viral load, it was found that the mean values of the tested sofosbuvir tablets in patients with low and moderate levels of viral load were significantly lower

($P < 0.001$) than those in patients with high viral load, where this trend was not observed.

Discussion

The special bioelectric properties of acupuncture points have attracted the attention of researchers as a means of localizing and analysing acupuncture points for diagnostic purposes. Various variants of commercial diagnostic devices related to the measurement of electrical skin resistance are being created [20, 21]. Numerous complicating factors associated with electrodermal acupuncture point measurements are described, such as dry skin, skin thickness, size of the sensitive electrode, electrode pressure, electrode spacing, room temperature, humidity and others [22, 23]. The results of research aimed at studying the relationship between electrical resistance of the skin in AP and various pathological conditions of the human body are described [24, 25]. The advantage of EAV diagnosis is the fact that its use for diagnostic purposes allows us to distinguish between two stages of the disease process: excess or deficient, which is the basis of the large holistic medical system of Chinese medicine and is crucial in the diagnostic process (Eight Principals). Higher EAV readings indicate energy excess or a tissue inflammatory stage, while lower readings suggest energy deficiency or a tissue degeneration stage. The EAV diagnosis allows medicament testing to be performed. The phenomenon of medicament testing discovered by Voll in 1954 raised many questions. It was suggested that the interaction of radiation of objects of living and non-living nature (drugs) was of electromagnetic origin when the electromagnetic oscillations of drugs interact with the frequency of oscillations of a biological object [26].From the standpoint of quantum physics, the effects of homoeopathic preparations are explained by the emission of weak nonionizing electromagnetic radiation of substances in supermall doses of preparation [27].However, the effects of allopathic drugs on the bioelectric properties of acupuncture points have not been described to date. Our study is pioneering in better understanding the potential of medicament testing methods for the selection of daily doses of the allopathic drug sofosbuvir, which can be applied to other drugs.

In the literature, we managed to find some information about the use of MT to determine the daily doses of drugs [28, 29]. Voll suggested using MT to determine the optimal dose of the medicine. For the first time, we proposed to use this technique for testing the daily doses of medicine [15]. In our opinion, the concept of a daily dose of a medicine accepted in traditional medicine reflects the concept of a standardised dose used to assess the drug consumption, rather than the dose at which the desired effect is achieved, which reflects the concept of an optimal dose of medicine.

Voll's innovation was that, as a result of his research, he succeeded in discovering many additional meridians, points of acupuncture and new functions of existing points, including the ability to use them for diagnostic purposes [30]. Voll's AP application on the existing Chinese meridians is not always the same as the Chinese AP. His new meridians are lymphatic system, nervous system, circulation, allergy, cellular metabolism, joints, fibroid tissue, skin and fatty tissue [17]. This accounts for 20 EAV meridians compared to 12 Chinese meridians.

Viral hepatitis C is one of the main causes of chronic liver diseases. Extrahepatic HCV replication is most likely associated with HCV damage to peripheral mononuclear cells, where HCV RNA can be stored for a long time, causing relapses of viral hepatitis after successful antiviral therapy and possibly providing chronization of the hepatitis C virus in the patient's body [31]. According to various authors, the detection of HCV RNA in peripheral blood mononuclear cells of patients with hepatitis C varies from 64 to 100% of cases [32]. It is believed that RNA of the virus is frequently registered in the blood cells of patients with more severe liver damage [33]. There are differing opinions on the relationship between viral load level and pathological process severity and between viral load level and histological activity index scores, histological sclerosis index, and ALT activity in patients with CHCV infection [34]. According to some researchers, viral replication increases as the disease progresses, and a higher level of viraemia correlates with more severe liver damage [35].

Conclusions

Despite its small sample size and low objectivity, this pilot study found a significant association between EAV electrodermal measurement of acupuncture points and tested daily doses of the antiviral drug sofosbuvir. Medicament testing for Xing-jian (LR2) and thoracic lymphatic duct (meridian circulation, Voll) can help to determine the daily doses of drugs in patients with CHCV infection. This finding suggests that acupuncture points may have diagnostic properties. To further assess the clinical applications and physiological basis of medicament testing methods, additional clinical and instrumental studies are needed with a large sample of patients.

Abbreviations

MT	Medicament testing
AP	Acupuncture point
CHCV	Chronic hepatitis C virus infection
EAV	Electroacupuncture according to Voll

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Author contributions
All authors were involved in concept, design, collection of data, interpretation, writing and critically revising the article. All authors approve final version of the article.

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Availability of data and materials
The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Declarations

Ethics approval and consent to participate
The study was approved by the Ethics Committee of the Ministry of Health of Uzbekistan (No 08/2,16.02.2011). All patients signed written informed consent form for the study.

Competing interests
The authors declare that they have no competing interests.

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References

1. Kramer S, Winterhalter K, Schober G, Becker U et al (2009) Characteristics of electrical skin resistance at acupuncture points in healthy humans. J Altern Complement Med 15(5):495–500. https://doi.org/10.1089/acm.2008.0331
2. Ahn AC, Martinsen OG (2007) Electrical characterization of acupuncture points: technical issues and challenges. J Altern Complement Med 13(8):817–824. https://doi.org/10.1089/acm.2007.7193
3. Colbert AP, Yun J, Larsen A, Edinger T, Gregory WL, Thong T (2008) Skin impedance measurements for acupuncture research: development of a continuous recording system. Evid Based Complement Altern Med 5(4):443–450. https://doi.org/10.1093/ecam/nem060
4. Kenyon JN (1983) Modern techniques of acupuncture: a practical scientific guide to electroacupuncture, vol I. Thoreson Publishers Inc, New York
5. Parsons G (2020) Hepatitis C: epidemiology, transmission and resentation. Prescriber 33(6):20–23. https://doi.org/10.1002/psb.1992
6. Luna-Cuadros M, Chen HW, Hanif H, Ali MJ, Khan MM, Lau DT (2022) Risk of hepatocellular carcinoma after hepatitis C virus cure. World J Gastroenterol 28(1):96–107. https://doi.org/10.3748/wjg.v28.i1.96
7. Recommendations for Testing, Managing, and Treating Hepatitis C. Joint panel from the American Association of the Study of Liver Diseases and the Infectious Diseases Society of America. http://www.hcvguidelines.org.
8. Stedman C (2014) Sofosbuvir, a NS5B polymerase inhibitor in the treatment of hepatitis C: a review of its clinical potential. Therap Adv Gastroenterol 7(3):131–40. https://doi.org/10.1177/1756283X13515825
9. Kindling Bioenergetic. https://www.kindling.de/produkt/vistron/Homopath_engl.pdf
10. Homopath_engl.pdf
11. Voll R (1997) Nosodenanwendung in Dignostik und Therapie. MLV-Uelzen
12. Leonhardt H (1980) Fundamentals of electroacupuncture according to Voll. Germany, Medizinisch Literarische Verlagsgesell schaft, Uelzen
13. Voll R (1980) The phenomenon of medicine testing in electroacupuncture according to Voll. Am J Acupunct 8:97–104
14. Rolik IS, Fursow SE, Fillipow AA (1993) Voll's method in diagnosis and therapy of chronic conditions. Gregory Electronics, Moskow, p 113
15. Patent NoIAP 03033 (2006) The method of determining the daily doses of medicines. Uzbekistan
16. Frosi A (2021) Extrahepatic manifestations of hepatitis C infection. In: Advances in hepatology. Open access peer-reviewed edited volume
17. Voll R (1983) The 850 EAV measurement points of the meridians and vessels including the secondary vessels. Medizinisch Literarische Verlagsgesellschaft, Uelzen
18. Tsibris AMN, Hirsch MS (2015) Antiretroviral therapy for human immunodeficiency virus infection. Mandel Douglas Benne's Princ Pract Infect Dis 1:1622–1641. https://doi.org/10.1016/B978-1-4557-4801-3.00130-2
19. Hajarizadeh B, Grebely J, Applegate T, Matthews GV, Amin J, Petoumenos K et al (2014) Dynamics of HCV RNA levels during acute hepatitis C virus infection. J Med Virol 86(10):1722–1729. https://doi.org/10.1002/jmv.24010
20. Ahn A, Martinsen Q (2007) Electrical characterization of acupuncture points: technical issues and challenges. J Altern Complement Med 13(8):817–824
21. Wong FW, Lim CE, Smith W (2010) A new bioimpedance research device (BIRD) for measuring the electrical impedance of acupuncture meridians. J Altern Complement Med 16(3):257–264. https://doi.org/10.1089/acm.2009.0218
22. Quintanilha SM, Cruz CP, Corso G (2011) The statistics of skin impedance. J Altern Complement Med 17(7):577–578. https://doi.org/10.1089/acm.2011.0157
23. Ma SX (2021) Low electrical resistance properties of acupoints: roles of NOergic signaling molecules and neuropeptides in skin electrical conductance. Chin J Integr Med 27(8):563–569. https://doi.org/10.1007/s11655-021-3318-5
24. Tseng YJ, Hu WL, Hung IL, Hsieh CJ, Hung YC (2014) Electrodermal screening of biologically active points for upper gastrointestinal bleeding. Amer J Chin Med 42(5):1111–1122. https://doi.org/10.1142/S0192415X14500694
25. Pontarollo F, Rapacioli G, Bellavite P (2010) Increase of electrodermal activity of heart meridian during physical exercise: the significance of electrical values in acupuncture and diagnostic importance. Complement Ther Clin Pract 16(3):149–153. https://doi.org/10.1016/j.ctcp.2010.01.004
26. Lupichev N (1996) Electropuncture diagnostics, homeopathy and the phenomenon of long-range action. Publishing house "Irius" (Russian)
27. Manzalini A, Galeazzi O (2019) Explaining homeopathy with quantum electrodynamics. Homeopathy 108:169–176
28. Djumaeva N, Djumaeva L (2011) The potential of the medicine testing technique in selection of the daily doses of medicines used to treat different infectious diseases. J Sci Heal Outcomes 3:7–10
29. Djumaeva N (2020) New approaches to diagnosis and therapy for Covid-19. All J Med Res 9:1–8. https://doi.org/10.14299/ijser.2020.09.04
30. Hong H (2016) Electrodermal measurement of acupuncture points may be a diagnostic tool for respiratory conditions; a retrospective chart review. Med Acupunt 28:137–147. https://doi.org/10.1089/acu.2016.1177
31. Su WC, Machida K, Lai MS (2016) Extrahepatic replication of HCV. In: Hepatits C virus II: infection and disease. Springer, pp 165–184
32. Grovatto M, Pozzato S, Zorat F et al (2000) Peripheral blood neutrophils from hepatitis C virus infected patients are replication sites of the virus. Haemotologica 85:356–361

33. Charlton M (2003) Liver biopsy, viral kinetics, and the impact of viremia on severity of hepatitis C virus recurrence. Liver Transpl 9(11):58–62. https://doi.org/10.1053/jlts.2003.50245
34. McCaughan GW, Shackel NA, Bertolino P, Bowen DG (2009) Molecular and cellular aspects of hepatitis C virus reinfection after liver transplantation: how the early phase impacts on outcomes. Transplantation 87(8):1105–1111. https://doi.org/10.1097/tp.0b013e31819dfa83
35. Alberti A, Tremolada F, Fattovich G, Bortolotti F, Realdi G (1983) Virus replication and liver disease in chronic hepatitis B virus infection. Dig Dis Sci 28(11):961–6. https://doi.org/10.1007/BF01311722

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