В таблице 2, максимальные зоны проявлялись в отношении Staphylococcus typhymurium, Staphylococcus albus. В целом антагонистическая активность данных культур составляет 17-21мм.

Таким образом, самая высокая кислотность молочнокислых бактерий наблюдалась на 4 штаммах (142-160^{0}Т). В данном случае антагонистическая активность зависит не только от образования молочной кислоты, но и от вида культуры.

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Жұмыста балық өнімдерінің, соның ішінде алабұға тұқымдас балықтан дайындалған фаршты сүтқышқылды микрофлорасы зертелінген.

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In this work the lactic flora of fish products, including fish mince prepared from sturgeon.

НАНОТЕХНОЛОГИЯ

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THE NEW NANOCAPSULES FOR SUCCESSFUL THERAPY OF SPINAL TUBERCULOSIS

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Our developed new nanocapsules very stable and never aggregate. These nanocapsules were loaded by four types antitubercular antibiotics. It was prepared the nanoointment by mixing loaded nanocapsules with lanoline. For the therapy of the spinal tuberculosis nanoointment was putted on the skin of the area of sick vertebras twice a day morning and evening. This kind of therapy accelerates the time of the curing and hundred times the quantity of the used antibiotics in comparison with traditional treatment.

According to the United Nations and the World Health Organization, more than two billion people, equal to one third of the world's total population, are infected with mycobacterium tuberculosis. One out of every ten of those people will have the active tuberculosis during his or her life [1] Unfortunately, this worldwide disease can not be controlled. It can be expected that success in fighting with this disease can be achieved by using methods of the nanomedicine.

Nanomedicine is created by the fusion of nanotechnology and medicine. It is one of the most promising pathways for the development of new strategies of the therapy of serious and widespread disease such as: tuberculosis [2-4]. One of the heaviest type of tuberculosis is the spinal tuberculosis, which often led to paraplegia[5].

The most promising method of nanomedicine for therapy of diseases are nanocarriers. Now there are two types of nanocarriers, first are natural nanocarriers and the second are polymer nanocarriers. The well-known drug delivery system are lecithin liposomes. These lecithin liposomes have serious disadvantages, because they have very large sizes and they easily aggregate. That cause the dangerous of the blocking blood vessels. The polymer nanocapsules cause numerous immune and allergic reactions. Because of these disadvantages both types of the delivery systems haven't found wide application in practical medicine. In general they are used for experiments on animals and model systems [6-8]. Thus, it is speaks about necessity to develop new nanocapsules from natural materials, which don't have above mentioned disadvantages.

The starting point of our investigation was our development of new effective methods of purification of phosphatidylinositol (PI) from plant materials. This method was protected by patent of US № 4,977,09[9] and by the patent of the Republic of Hungary №199 691[10]. In contrast to all other electroneutral phospholipids, PI has a negative charge. In this respect PI is very convenient for the construction of charged small liposomes, which were stable in buffer solution. We have developed the method of preparation of PI liposomes protected by the patent of the Republic of Kazakhstan [11]. Our obtained PI liposomes not visible in optical microscope this indicates that their sizes less than one mkm. In this reason we named PI liposomes as nanocapsules. In contrast

to electroneutral the lecithin liposomes our nanocapsules thanks of their negative charge push each other and they never aggregate and never agglomerate. Our study shows that the nanocapsules are very stable in wide ranges of ph from 5 till 9 and temperature from -30 till +55. The nanocapsules can be stored without any changes for several years in sterile conditions.

We also developed the effective method of the loading nanocapsules by different medicines. The principle of our method is in the next: the nanocapsule is opened in hydrophobic solution (95,6% ethanol) like a shell.

Then nanocapsules are transferred to the hydrophilic solution (0.05M Tris-HCl buffer ph 7.4), they begin to close scooped the solution containing medicines. So, we have proposed the new method which provides a very high efficiency of loading the nanocapsules. This method protected by patent of the Republic of Kazakhstan №17043[11].

For preparation of nano ointment the nanocapsules were loaded by the next antitubercular antibiotics: isoniazid, rifampin, pyrazinamide and ethambutol. Then the solution with loaded nanocapsules were mixed in equal proportion with lanoline. The prepared nano ointment was used for the therapy of the spinal tuberculosis.

In June 2009, one of the authors of this article Gilmanov Murat fell ill with spinal tuberculosis. In August 3, 2009 Gilmanov was happened paralysis of the bottom part of the body and legs – paraplegia, as a result of this disease, the infection destroys the 4-5th bone of vertebras, that leads to the destruction of spinal neural cord, as you can see on the photo (fig.1) of the magnetic resonance tomography of September 2, 2009.

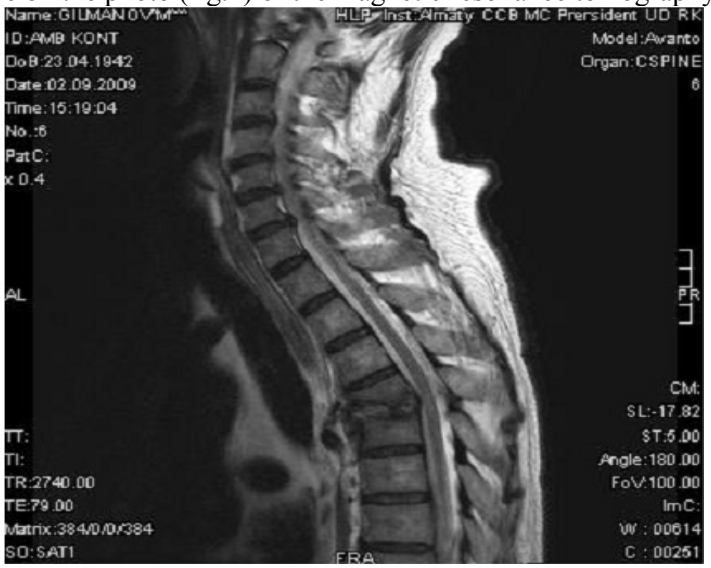

Fig.*1. The tomography was carried out on magnetic resonance tomograph type 1.5Тл MAGNETOM Avanto "Siemens AG" (Germany). The height of the vertebral bodies decreased, the bone of 4.-5. vertebras destructed and the space between them is filled with purulence. Spinal canal is narrowed between 4.-5. vertebras, with partial spinal cord compression due to epidural abscess up to 5 mm.*

Conclusion: MRT data spinal tuberculosis of 4.-5. vertebras complicated by epidural and paravertebral abscess at this level.

On August 10, 2009, the epicystostoma was sewn to his urinary bladder. Then, Gilmanov received treatment at the clinic under the supervision of an experienced phthisiatrician, doctor Tutkishbaev C.O. in the National Centre for Problems of Tuberculosis (Almaty). The extract from the patient's history is presented here.

On September 9, 2009, Gilmanov Murat was admitted as a patient of the National Centre for Problems of Tuberculosis of the Republic of Kazakhstan (Almaty) in accordance with his diagnosis - tubercular spondylitis (spinal tuberculosis). By the decision №141 of September 10, 2009 of the medical commission the patient was recommended the therapy by tablets of the first-line antibiotics: isoniazid, rifampin, pyrazinamide and ethambutol. However, Gilmanov Murat refused to receive per oral treatment of these antibiotics. He decided to test thetherapyt by own nano ointments. For that Gilmanov's colleagues prepared 4 types of nano ointments with four above mentioned antibiotics. From September 17, 2009 these ointments were rubbed on the skin in the area of sick vertebras in short intervals in the morning and in the evening everyday. After 50 days of this treatment the magnetic resonance tomography shows the improvement of the state of the damaged vertebras , as it shown at fig.2.

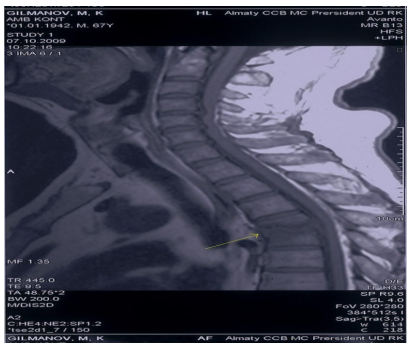

Fig.2. The tomography was carried out on magnetic resonance tomograph type 1.5Тл MAGNETO Avanto "Siemens AG" (Germany). There is positive dynamics and disappearance of purulence.

By November 20, 2009, after therapy by nano ointment, some neurological functions of several organs and legs of the patient were restored, and his epicystostoma was removed. By December 25, 2009 it was completely stopped applying the ointment on the spine of Gilmanov. Gilmanov was prescribed massage and physical exercises therapy. Considering clinical and roentgenological positive dynamics of the therapy, Gilmanov Murat was discharged from the Centre in the satisfactory condition on the 21-st of January, 2010.

Thus, instead of 9 months of traditional therapy by tablets of antibiotics Gilmanov M.K. was full cured within 3 months by nanoointment therapy. After one year of the therapy Gilmanov M.K. had no relapse of spinal tuberculosis, and gradually were restored all motor functions of the legs.

Therefore, our nanocapsules loaded by antitubercular antibiotics for therapy of tubercular spondylitis allow to reduce: the duration of the therapy three times and hundreds times the quantity of the used antibiotics. It's clear by the next calculation under the traditional therapy Gilmanov must to take more than 4000 tablets of antibiotics (16 tablets everyday during 9months). For the therapy by our nanocapsules was spent only 20 tablets for preparation nanoointments for full time of the therapy. The very big advantage of the therapy of spinal tuberculosis by nano ointment is the absence of the toxic effects on other health organs. All this reduces several times the cost of treatment with a better therapeutic effect. Thus, our developed nanoointments are successful for therapy very serious disease - tuberculous spondilytis . Now our nanocapsules loaded by antitubercular antibiotics are testing for therapy of lung tuberculosis in the National Centre for Problems of Tuberculosis (Almaty).

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Разработанные нами нанокапсулы очень стабильны и не обладают способностью к агрегации. Эти нанокапсулы были загружены четырьмя видами противотуберкулезных антибиотиков. Была подготовлена наномазь путем смешивания загруженных нанокапсул с ланолином. Для лечения туберкулеза позвонков наномазь наносилась на кожу в области больных позвонков дважды в сутки утром и вечером. Этот вид терапии ускоряет время излечения четыре раза и количество используемых антибиотиков уменьшает в сотни раз по сравнению с традиционным лечением.

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Біз зерттеп шығарған нанокапсулалар өте тұрақты және бір-біріне жабыспайды. Төрт түрлі туберкулезге қарсы антибиотиктер осы нанокапсулаларға жүктелді. Жүктелген нанокапсулаларды ланолинмен араластыру арқылы нано май алынды. Омыртқалар туберкулезін емдеу үшін наномай тәулігіне екі рет таңертең және кешке ауру омыртқалар аймағындағы теріге жағылады. Емдеудің бұл әдісі дәстүрлі әдіске қарағанда емдеу уақытын 4 есе, ал қолданылатын антибиотиктердің мөлшерін 100 есе азайтады.