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ORIGINAL ARTICLE

THE NEED FOR IMPROVEMENT OF FUNGICIDES RESIDUAL QUANTITIES CONTROL METHODS IN THE CONDITIONS OF THE DOMESTIC REGULATORY BASE HARMONIZATION

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Sergii T. Omelchuk, Alina I. Syrota, Anna V. Blagaia

BOGOMOLETS NATIONAL MEDICAL UNIVERSITY, KYIV, UKRAINE

ABSTRACT

The aim: To develop highly sensitive analytical methods for the determination of the systemic phenylamide class fungicide – Metalaxyl-M residues in watermelons and grapes to reduce the risk of hazardous effects on workers' and public health.

Materials and methods: Conditions for Metalaxyl-M detection by gas-liquid chromatography (GLC) using a chromatographic capillary column SH-Rxi-5ms (length – 30 m, inner diameter – 0.25 mm, layer thickness – 0.25 µm) were determined. The optimal conditions for chromatography of Metalaxyl-M were established: column thermostat temperature – 220°C, evaporator temperature – 260 °C, detector temperature – 280 °C. The retention time under these conditions was 3,384 ± 0.1 minutes. The linear detection range is 0.01 to 0.05 mg / kg. The calibration dependence of the tested substance peak area on its concentration was established and described by the linear regression equation.

Results: We found that the most sensitive method for chromatography of Metalaxyl-M is the method of using a capillary column SH-Rxi-5ms on a gas chromatograph Shimadzu Nexis 2030.

Conclusions: The developed GC methods correspond to modern requirements, are selective and allow to control the Metalaxyl-M content in the matrices of the studied crops and can be used as a marker of the safety of agricultural products grown with fungicides containing Metalaxyl-M application. We found that the most sensitive method for Metalaxyl-M chromatography detection is the method with usage of a capillary column SH-Rxi-5ms on a gas chromatograph Shimadzu Nexis 2030.

KEY WORDS: metalaxyl-M, gas-liquid chromatography, fungicides, phenylamides, berry crops

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INTRODUCTION

As preventive measures aimed at preventing the negative impact of pesticides on human health and the environment, at the stage of pre-registration testing, it is mandatory to optimize and improve the methods of analytical determination of their residual amounts in the studied crops.

As of 2021, fungicides occupy a leading place in the list of the State Register of Pesticides and Agrochemicals Allowed for Application in Ukraine, including about 30 formulations based on phenylamide compounds and about 10 with the active substance Metalaxyl-M [1, 2].

Today high-performance liquid and gas-liquid types of chromatography are used in Ukraine to determine the residual amounts of pesticides in agricultural raw materials [3-5].

In particular, modern sensitive and effective methods for quantification of Metalaxyl-M residual amounts have been developed, involving the usage of gas chromatography with Nitrogen-Phosphorus Detector (NTD) and gas chromatography with mass spectrometry (GC-MS) [6].

Methods for detecting Metalaxyl-M residual amounts in grapes and watermelons approved in Ukraine were developed in 2000 and 2014, respectively.

The importation into the EU of agricultural products containing pesticide residues above 0.01 mg/kg will be

prohibited since May 2020, according to the EU decision on reduce the maximum allowable levels of certain pesticides in agricultural and food products, and establishment of new standards that will apply to both food products produced in the EU and imports [7].

In Ukraine, the Commission on Integrated Hygienic Standardization and Regulation of Pesticides and Agrochemicals of the State Enterprise «Committee on Hygienic Regulation of the Ministry of Health of Ukraine» examines materials on the scientific substantiation of hygienic standards and regulations for safe pesticides application under the requirements of Resolution 04.03.1996 №295 «On approval of the Procedure for conducting state tests, state registration and re-registration, publication of lists of pesticides and agrochemicals permitted for usage in Ukraine». Institutions of the toxicological and hygienic profile of the Ministry of Health and the National Academy of Medical Sciences of Ukraine accredited for the right to carry out work in the field of hygienic regulation of pesticides in industrial and environmental facilities substantiate hygienic standards [8].

Concerning hygienic standards, particularly maximum allowable levels (MALs) of pesticide content in products, such standards are substantiated and approved in the man-

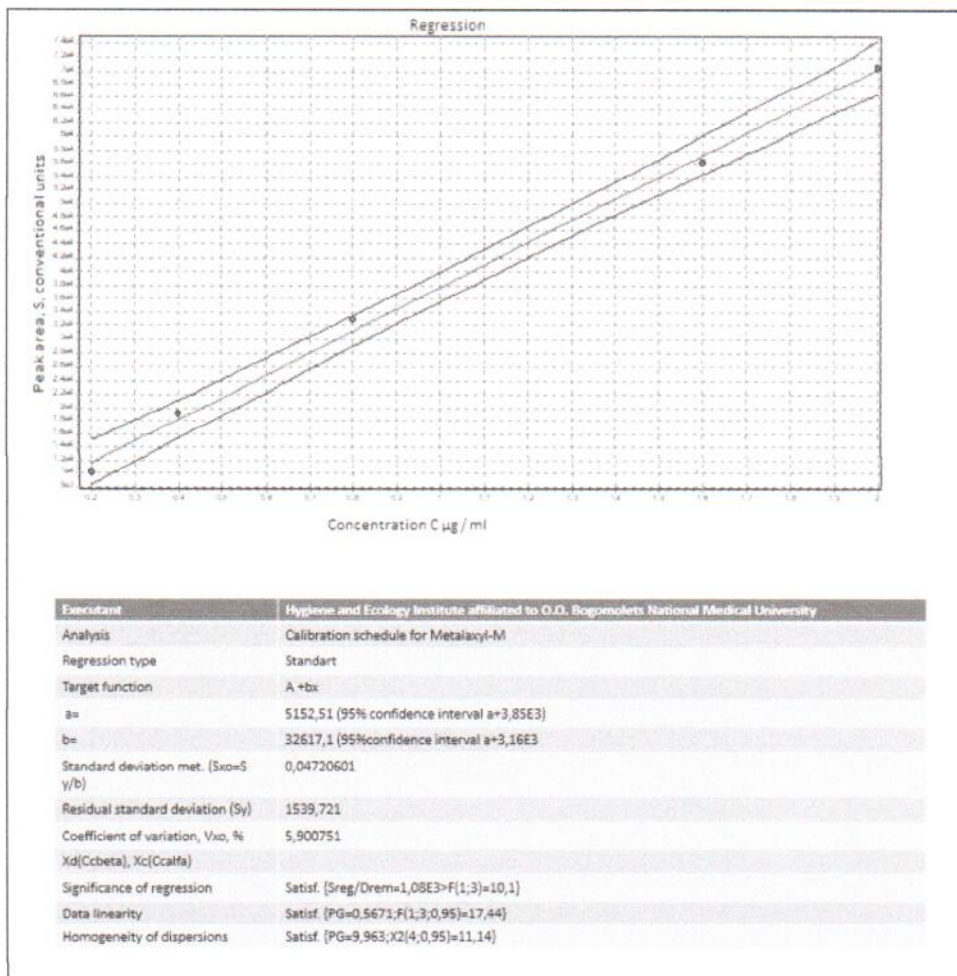


Fig 1. Diagram of the dependence of the Metalaxyl-M chromatographic peak height (conventional units) from the concentration of Metalaxyl-M in the calibration solution ($\mu\text{g/ml}$)

ner prescribed by applicable law, methods of their control are developed, and the risk of residues is assessed.

However, the approved maximum residue levels of these active substances in some crops significantly exceed the standard recommended by the European Commission at the level of 0.01 mg/kg.

Therefore, it is possible to limit the content of Metalaxyl-M residues in products from 0.04 mg/kg to the level of 0.01 mg/kg only if the existing standards in Ukraine are revised and (if necessary) the MALs is approved at the level of 0.01 mg/kg, which provides for an increase sensitivity of the method [9].

This issue can be resolved only in compliance with the procedure of approval of hygienic standards and regulations in the manner prescribed by applicable law, in compliance with the requirements of Law №86 / 95-VR, Resolution of the Cabinet of Ministers of Ukraine № 420 of 13.06.1995 and other regulation documents, regulating the safety of pesticides at the stage of their post-registration usage [10, 11].

That is why as the purpose of our work we have chosen the development of analytical methods for the determination of Metalaxyl-M in berry crops to improve the quality of control and safety of consumption of products grown with usage of fungicides based on compounds of the phenylamide class.

THE AIM

Aim of the work: the development of highly sensitive analytical methods for the determination of residues levels of the phenylamide class systemic fungicide – Metalaxyl-M in watermelons and grapes to reduce the risk of dangerous effects on the workers' and public health.

MATERIALS AND METHODS

To establish the optimal conditions for chromatographic detection of Metalaxyl-M, we conducted a series of experiments. Selection of optimal gas-liquid chromatography conditions was performed using Shimadzu Nexis GC-2030 and GC-2014 gas chromatographs equipped with SH-Rxi-5ms capillary columns. The study was performed at different column temperatures in the range of 220-260 °C. Data on the physicochemical properties of Metalaxyl-M are shown in table I.

RESULTS

To establish the optimal conditions for chromatography detection of Metalaxyl-M, shown in table II, a series of experiments were performed at the previous stage. Selection of optimal conditions for gas-liquid chromatography was performed using the above-mentioned Shimadzu

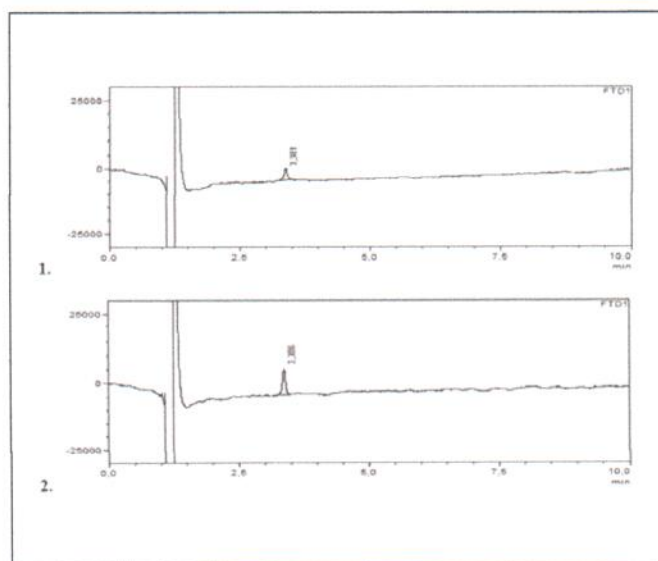


Fig 2. Chromatograms of Metalaxyl-M calibration solutions with concentrations:

1 – 0.4 µg/ml

2 – 0.8 µg/ml

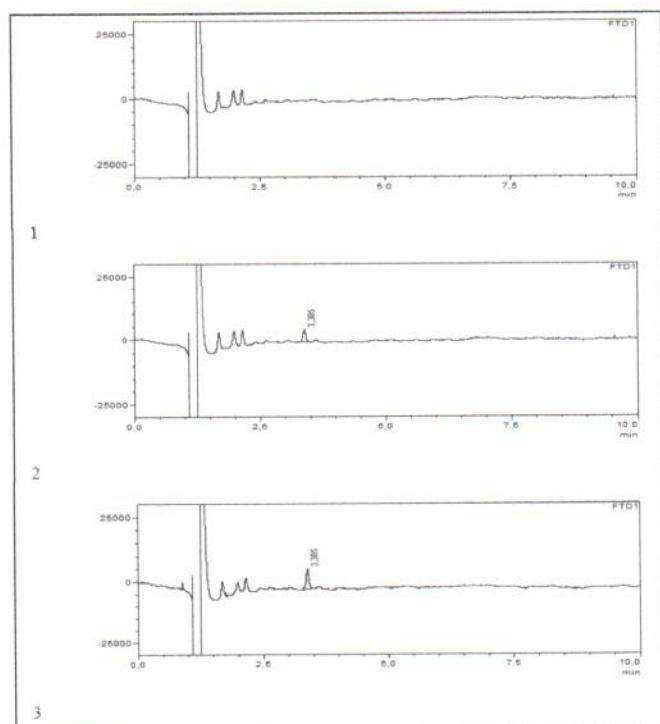


Fig. 4. Chromatograms of grape sample extracts

1 – control sample (1 µg/ 1ml / 40g);

2 – model test with the introduction of Metalaxyl-M 0.01mg/kg (1 µg/ 1ml / 40g)

3 – model test with the introduction of Metalaxyl-M 0.02mg/kg (1 µg/ 1ml / 40g)

gas chromatographs. Each time the work began with the construction of a calibration diagram, according to the international standard [12], which revealed the relationship between the peak area and the Metalaxyl-M concentration.

The next stage of the laboratory experiment was the selection of reagents for Metalaxyl- M extraction from

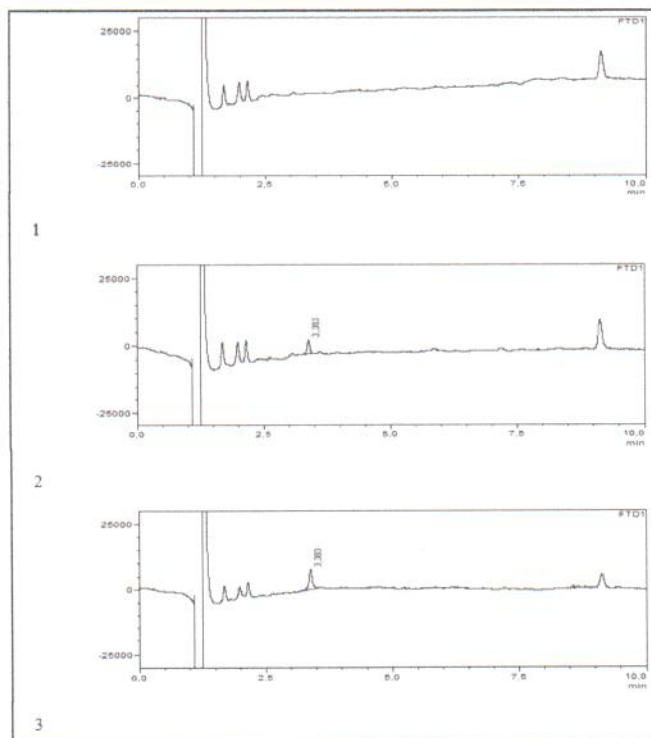


Fig 3. Chromatograms of watermelon samples extracts

1 – control sample (1 µg/ 1ml / 40g);

2 – model test with the introduction of Metalaxyl-M 0.01mg/kg (1 µg/ 1ml / 40g)

3 – model test with the introduction of Metalaxyl-M 0.02mg/kg (1 µg/ 1ml / 40g)

samples of the studied crops, as well as sequential purification of samples of the obtained extract by redistribution in the liquid-liquid system and purification by solid phase extraction (SPE). When choosing extractants for the Metalaxyl-M determination in watermelons and grapes, the best result was achieved using an extraction mixture of hexane + acetone (1 + 1, volume + volume). Also, at the stage of extractants selection, hydrochloric acid, sodium hydroxide, chloroform, a mixture of hexane + diethyl ether (1 + 1, volume + volume) were used.

The studies allowed to establish the optimal conditions of extraction and purification, which provided a selective Metalaxyl-M determination from matrices without impurities, which did not interfere with its chromatographic determination.

Before chromatography detection, the obtained extracts were filtered through a filter "blue tape" into a 250 ml volumetric flask. The extraction was repeated twice. The residue on the filter was washed with 10 ml of hexane + acetone extraction mixture. The combined filtrate for distilling off the solvents was transferred to a 250 ml pear-shaped flask and evaporated on a rotary evaporator at a water bath temperature not exceeding 40° C to the aqueous residue.

The aqueous residue of watermelon and grape samples was transferred to a separating funnel with a capacity of 250 ml. The flask was washed with 10 ml of acetone and transferred to a separatory funnel. There was added 20 ml of hydrochloric acid (0.1 mol), mixed thoroughly and

Table I. Physicochemical properties of Metalaxyl-M

Index	Value	
Chemical name (IUPAC)	(R)-2[(2,6-dimethylphenyl)-methoxy-acetylamino]-propionic acid methyl ester	
CAS RN	70630-17-0	
Empirical formula	C ₁₅ H ₂₁ NO ₄	
Relative molecular mass	279.3	
Structure formula		
Vapor pressure, mPa (20 °C)	3,3×10 ⁻³	
Solubility in water, mg / dm ³ (25 °C)	26	
Solubility in organic solvents, g / dm ³ (20 °C)	n-hexane	59
Partition coefficient Log Po/w (25°C)	1,71	

Table II. Conditions for chromatography detection of Metalaxyl-M

Characteristics of the method for determining	Metalaxyl-M	
	GC	
Chromatograph	Gas-liquid chromatograph «Nexis GC-2030», «Shimadzu»	
Detector	thermoionic detector	
Column	capillary column SH-Rxi-5ms, length - 30 m, inner diameter - 0.25 mm, layer thickness - 0.25 µm	
Volumetric flow rate of carrier gas (helium), ml/min	20.6±1	
Column thermostat temperature, °C	220±1	
Evaporator temperature, °C	260±1	
Detector thermostat temperature, °C	280±1	
Liquid chromatograph injector loop volume, µl	1	
Retention time under these conditions, minutes	3.384±0.1	
Linear detection range, µg / cm ³	0.2-2	
Dependence of the area of the chromatographic peak (S) of metalaxyl-M (units) on its concentration (ρ) in the calibration solution (µg/cm ³)	S Metalaxyl-M = 5152,51+32617.1×ρ	

the pH of the solution was adjusted to 5-6 with sodium hydroxide (1 mol). It was then extracted three times with chloroform in 20 ml portions and shaken for (1-2) minutes. After phase separation, the lower (chloroform) layer was collected in a 250 ml volumetric flask and dried by infusion over 20-25 g of anhydrous sodium sulfate, stirring periodically for 20 minutes. The extract separated from the precipitate by decantation was then poured into a 100 ml pear-shaped solvent distillation flask and evaporated on a rotary evaporator at a water bath temperature of not more than 40 °C to a volume of ~ 0.5 ml. The solvent was evaporated to dryness by a stream of dry air.

The dry residue obtained after evaporation was washed with 5 ml of hexane + diethyl ether and passed through a Strata[®]NH₂ cartridge using a vacuum solid phase extraction system. The filtrate was collected in a 25 ml pear-shaped flask. The speed of passing the sample through the cartridge was 5-7 ml/min (preventing drying of the cartridge surface!). The cartridge was washed with 5 ml of a mixture of hexane + diethyl ether, adding the solvent to the main extract. The combined filtrate was evaporated on a rotary evaporator at a water bath temperature not exceeding 40 °C to a volume of ~ 0.5 ml. The solvent was evaporated to dryness by a stream of dry air. The resulting

Table III. Metrological characteristics of Metalaxyl-M determination in grapes

Object of analysis		Grapes			
Sample, grams		40			
Added Metalaxyl-M, mg/kg	Detected Metalaxyl-M, X _{ij} , mg/kg	Detected Metalaxyl-M, R _{ij} , %	Detected, R _{ij} , %	Standard deviation of single concentration, (n=6), S _{ij} , %	Confidence interval of single concentration, ± %
0.4	0.0089	88.6	92.1	3.28	3.44
	0.0096	96.2			
	0.0093	92.5			
	0.0089	88.8			
	0.0094	94.4			
	0.0093	92.6			
0.8	0.0175	87.5	86.0	3.16	3.32
	0.0166	83.2			
	0.0177	88.7			
	0.0178	89.2			
	0.0169	84.4			
	0.0167	83.4			
The average value of the definition, R, %				88.9	
Standard deviation (n=12), S, %				4.7	
Confidence interval (p=0,95), ± %				3.0	
Limit of determination, mg / kg				0.4	

Table IV. Metrological characteristics of determination of Metalaxyl-M in watermelon

Object of analysis		Watermelon			
Sample, grams		40			
Added Metalaxyl-M, mg/kg	Detected Metalaxyl-M, X _{ij} , mg/kg	Detected Metalaxyl-M, R _{ij} , %	Detected, R _{ij} , %	Standard deviation of single concentration, (n=6), S _{ij} , %	Confidence interval of single concentration, ± %
0.4	0.0091	91.1	92.7	1.45	1.52
	0.0094	94.0			
	0.0094	93.6			
	0.0092	92.4			
	0.0094	94.1			
	0.0091	91.3			
0.8	0.0181	90.5	90.0	1.60	1.68
	0.0179	89.5			
	0.0178	89.0			
	0.0183	91.7			
	0.0176	88.0			
	0.0183	91.4			
The average value of the definition, R, %				91.3	
Standard deviation (n=12), S, %				2.1	
Confidence interval (P=0,95), ± %				1.33	
Limit of determination, mg / kg				0.4	

dry residue was transferred to a 10 ml graduated tube with acetone (final sample extract volume 1 ml). A parallel sample was prepared similarly. The schedule of the dependence of the Metalaxyl-M chromatographic peak height on the concentration in the calibration solution is shown in Fig. 1.

Metrological characteristics of the Metalaxyl-M determination in agricultural raw materials, like watermelons and grapes are given in tables III, IV.

Chromatograms of Metalaxyl-M standard solutions, sample extracts with the introduction of Metalaxyl-M in watermelons and grapes are shown in Figure 2,3,4.

According to the data shown in tables III and IV, the average value of the Metalaxyl-M determined concentrations in different matrices was not less than 70 %, which corresponds to modern requirements [13].

DISCUSSION

We conducted a study of literary data and scientific works regarding the conditions of chromatography, extraction and methods of analysis of materials for Metalaxyl-M. Unlike our sample preparation the extraction in the case of European colleagues for high moisture content crops like grapes and watermelons looks different. For example, on the first steps of preparation: they took 25g of the finely chopped sample and added 250 ml of 20 % water+methanol and blended the sample for 10 minutes on slow speed. At the same time, we took 40 grams of the sample and found the best results with extraction mixture of hexane + acetone.

Their next step was to filter the extract through a Whatman 2V filter paper into a 16-oz. bottle. In our case the obtained extracts were filtered through a filter "blue tape" into a 250ml volumetric flask. After that they transferred a 54 ml aliquot (5 g equivalent) and concentrated to a small volume (approximately 10 ml) using evaporator (bath temperature 40 degrees). After that 100 ml of 85% phosphoric acid, approximately 1 g of cobalt chloride hexahydrate and 2-3 boiling chips were added to the flask containing the sample. The flask was boiled to the point 170 degrees. We avoided the step with boiling and instead after the evaporation phase of preparation after the transfer with acetone to the separators funnel was added 20 ml of hydrochloride acid and mixed with sodium hydroxide to adjust the pH.

Then their description of following steps includes cooling and adding distilled water, adding sodium hydroxide solution, rinsing the condenser with water, steam distillation and alumina column cleanup which is perfectly described in the materials. And after that samples are ready for GC analysis.

In general, to describe the methods and sample preparation stages, we should admit that EU variant contains more stages and our is more simplified. The proportions and reagents we were using has some differences. But in the end, we can see the result that corresponding.

In their results plant samples fortified at 0.05 to 0.40 ppm showed recoveries ranging from 53 to 95% with an average recovery of 72 + 11% (n = 18). While our results

had shown that the average value of the Metalaxyl-M determined concentrations in different matrices (watermelons and grapes) was 88.9- 91.3 %, which corresponds to modern requirements and the same studies in other countries of EU.

Gas chromatographic method was used for the determination of total residues of Metalaxyl-M in crops in both cases. They were using Tracor 200 GC-AFID analysis (with alkali flame ionization detector) and Finnigan Model 3200 GC-MS analysis while we were using Shimadzu Nexis GC-2030 and GC-2014 with flame thermionic detector (FTD) with suitable temperatures and settings [14, 15].

CONCLUSIONS

The developed GC methods correspond to modern requirements, are selective and allow to control the Metalaxyl-M content in the matrices of the studied crops and can be used as a marker of the safety of agricultural products grown with fungicides containing Metalaxyl-M application. We found that the most sensitive method for Metalaxyl-M chromatography detection is the method with usage of a capillary column SH-Rxi-5ms on a gas chromatograph Shimadzu Nexis 2030.

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ORCID and contributionship:

Sergii T. Omelchuk: 0000-0003-3678-4241 ^{A,G,F}

Alina I. Syrota: 0000-0003-2161-8048 ^{B-D}

Anna V. Blagaia: 0000-0002-2451-9689 ^E

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Anna V. Blagaia

Bogomolets National Medical University

13 T. Shevchenko blvd., 01601 Kyiv, Ukraine

tel: +380503523399

e-mail: profilactika@hotmail.com

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