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STRENGTHENING RESEARCH ON NON-TOXIC INSECTICIDES

DP/HUN/82/006

HUNGARY

Terminal report *

Prepared for the Government of the Hungarian People's Republic
by the United Nations Industrial Development Organization,
acting as executing agency for the United Nations Development Programme

Based on the work of Prof. Dr. György Matolcsy

Backstopping officer: S. Sazonov, Chemical Industries Branch

United Nations Industrial Development Organization
Vienna

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V.87 82423

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A/ Development problems and immediate problem(s) attacked.

The development objective was to contribute to worldwide efforts aimed at eliminating the presently used traditional and toxic insecticides which create permanent threat to human beings, useful organisms and to the environment; to replace them with selective chemicals acting only against the target organisms.

This objective was also related to the Decision of the Council of Ministers 3.419/80 on the "Central Development Programme on the Production of Pharmaceuticals, Pesticides and Intermediates", as well as to the Decision of Council of Ministers 2.025/1980 on "Research and Development of Pesticides".

The basic consideration serving as justification for the research and development activity within the project was that the

introduction of novel type selective chemicals into the agricultural and sanitary insect control could eliminate one of the major hazards originating from presently used traditional insecticides, namely their toxic action against humans and useful non target organisms as well as environmental contamination.

It was to be considered, that in the pesticide industry representing the predominant part of world wide pesticide research capacity, the research on non-traditional insecticides is much less intensive than justified by its importance. This is explained partly by the fact that some of the novel type of anti-insect agents could be used at very low dosages, which in turn would make their commercialization by transnational industries non-profitable. Therefore scientific institutions, representing a minor research potential must undertake to a larger extent the responsibility for this problem of global importance. Because of the limited number of research teams working on insect hormone analogs and anti-hormones, the intensified research activity supported by UNDP assistance created a notable contribution to world-wide efforts on this field.

The <u>immediate objective</u> was to strengthen the actual research and development activity on novel type insecticides at the Research Institute for Plant Protection of the Hungarian Academy of Sciences. In order to achieve this, a new organic chemistry and a biochemistry laboratory was to be built and the staff (Appendix 6.) to be trained on the effective utilization of up-to-date research techniques.

The activities aimed at achieving these objectives were to be carried out on three different levels: 1/ research and development; 2/ investment; 3/ training. If appropriate the items B - C will be discussed according to these activities.

Research and development were planned to be supported by subcontracts (Appendix 5.) to assay the chemicals prepared within the project for detailed biological and biochemical activity in institutions representing top level in the relevant field.

A significant increase of research capacity was planned by the acquisition of new laboratory equipment (see investment);

Study tours and fellowship programmes were organized to train the staff and to establish international co-operations in order to extend and intensify research activity (see training).

B/ Outputs produced and problem(s) encountered.

1/ Research and development

As a result of the research and development work during the project 298 new compounds - expected to act as selective anti-insect agents - were designed, synthesized and assayed for their biological activities (Appendix. 1.).

During the project 10 papers were published and 10 lectures were presented on different occasions and one patent application was made (Appendix 2.).

Two foreign and three domestic subcontractors (see Appendix 5.) contributed to the project (see item C/1/).

One of the domestic subcontractors (see Appendix 5.2.3.) made

the elementary analysis for the determination of the structure of the synthesized compounds.

2/ Investment

Two new laboratory complexes, an organic chemistry and a biochemistry complex have been built and fully equipped with up-to-date laboratory equipment. Besides, the equipment of the already existing old laboratories has been complet 1 with new facilities (see Appendix 4.).

These laboratories and new instruments are the following:

a) A new complex of organic chemistry laboratories equipped with up-to-date facilities for the synthesis of the compounds, separation and structure determination;

b) A complex of biochemistry laboratories for studying the mechanism of action of the compounds at biochemistry level.

c) A nuclear magnetic resonance (NMR) spectroscope aimed at structure determination of the prepared compounds has been purchased and installed in the organic chemistry unit.

d) A high performance liquid chromatograph (HPLC) has been purchased and installed in the new biochemistry laboratory unit.

3/ Training

Three long term fellowship programs were completed and a fourth is in progress and is to be terminated in february 1987 (Appendix 3.1.). Reports have been submitted. Staff members has completed a number of study tours and participated on scientific conferences (see Appendix 3.2.) delivering lectures on results achieved in the project (see Progress reports submitted.). These activities were regarded on the one hand as part of the training program on the other hand they served presentation of the results achieved within the project.

C/ Objectives achieved or likely to be achieved in the near future

1/ Research and development

As a result of the project three new chemical types of selective anti-insect agents have been developed, which held promise to satisfy the immediate and long term objectives of the project. Two of the new types represent juvenile-hormone analogues, the third insect chitin synthesis inhibitory benzoyl-biuret derivatives. Steps are being undertaken for further development and/or to submit these chemicals for practical development by the Hungarian chemical industry by creating the necessary engineering, registrational, patent, commercial and other conditions.

The new-anti insect agents selected for further development were the results of an extensive molecular design, chemical synthesis and biological screening activity in the course of which 298 new compounds were synthesized (Appendix 1.). These compounds belong to the class of the IV. generation selective anti-insect agents, such as anti-juvenile hormones, chitin synthesis inhibitors, which disturb insect growth and development, and to the modern environmentally safe and selective insecticides.

The results achieved during the project has been published or going to be published in papers or presented in lectures (see Appendix 2.). Details of the most important research activities of the project are given below:

High juvenile hormone (JH) activity was demonstrated in case of six new synthetic compounds. The bioactivity of these juvenoids were superior to fenoxycarb, a commercial juvenoid insecticide (see Appendix 2.2.10.). Patent application was made for the protection of the discovery (see Appendix 2.3.), and steps are being made for the practical development of the best derivative.

Novel insect growth regulatory activity of alkylenebis-isothiocyanates was discovered (see Appendices 2.1.6. and 2.2.4.). These compounds inhibit the spiracle- and crochet-formation of the developing insect larvae thus rendering them non-viable. This symptom and the metabolic background has been studied also on subcontract basis [see Appendix 5.1.(Riddiford)

and 5.2.1 (Kiss)]. The Hungarian subcontractor measured the inhibition of the incorporation of labeled ^{3}H-tyrozine in Locusta migratoria by some of the bisisothiocyanate and dithiocarboxylate derivatives.

Compounds were designed, synthesized and tested as potential anti-moulting agents (chitin synthesis inhibitors). For the design computerized quantitative structure-activity relationship (QSAR) approaches were also applied. One of the outcome of this line was the discovery of a new class of chitin synthesis inhibitors, the benzoylbiuret derivatives (see Appendix 2.2.5.).

Field tests of formulations of the new synthetic juvenoid compounds were carried out on larvae of fall webworm. Under field conditions the new juvenoids proved to be as efficient as fenoxycarb.

New compounds synthesized in the Plant Protection Institute were evaluated on subcontract basis in biological assays of juvenile hormone biosynthesis, egg growth and microsomal mixed-function oxidase activities in insects [see Appendix 5.1.2. (Feyereisen)]. A cyclopropylbenzamide derivative was found to be a good inhibitor of juvenile hormone biosynthesis, an imidazole analogue of metyrapone was good inhibitor of microsomal mixed-function oxidases and a further compound was a moderate inhibitor of egg growth (see Appendices 2.1.1., 2.1.8. and 2.2.10.).

Compounds were regularly screened for anti-juvenile hormone activity using the larvae of Oncopeltus fasciatus, Hyphantria cunea, Heliothis maritima, and Pieris brassicae. Some of the

compounds were highly toxic on the insects, but none of them showed specific morphogenetic anti-JH activity.

A comparative study was made on the JH activities of different formulations of juvenoid compounds on bug species in order to enhance field stability. Micro-encapsulated formulations had the highest activity.

Compounds were screened for anti-sclerotizing activity on the larvae of Sarcophaga bullata. None of the compounds had noticeable effect on the structure of puparial cuticle.

The evaluation of certain compounds were also made on subcontract basis [see Appendix 5.2.1.(Kiss)]. The compounds distu. bed normal metamorphosis of the larvae of Locusta migratoria with lethal outcome. The compounds probably disturbed the normal functioning of acetyl-dopamine, an important intermedier for the cuticle biosynthesis.

A novel effect of the beta-alanine derivatives was discovered influencing the coloration of the pupal cuticle of Sarcophaga bullata and Mamestra brassicae. The compounds probably interfere with beta-alanine biosynthesis (see Appendices 2.2.3. and 2.2.8.).

Domestic subcontractor [see Appendix 5.2.2.(Radványiné)] evaluated four compounds synthesized in the Plant Protection Institute on Musca domestica (house fly) as potential MAO inhibitors. The compounds were less active than the standard MAO inhibitors (deprenil, dimilin).

Domestic subcontractor [see Appendix 5.2.2.(Radványiné)]

developed a quantitative electrophysiological method for the evaluation of the neurotoxicological activity of pyrethroid derivatives using prepared Blabera craniifer (cockroach) nerves. Six new pyrethroid analogue synthesized in the Plant Protection Institute were tested by this method. The compounds proved to be ineffective. In the long run the new method is a valuable tool for the screening of candidate pyrethroids.

Compounds of various chemical structure were assayed for chemosterilant activity using Dysdercus cingulatus and Planococcus citri. Weak or moderate chemosterilant activity was found in 14 compounds (see Appendices 2.1.1. and 2.1.7).

In a study comparison was made between the chemosterilant and juvenile hormone activity of some soft-alkylating agents using Dysdercus cingulatus and Pieris brasiicae. While the chloro-methyl-esters of the dodecadienoate type juvenoids exerted considerable chemosterilant activity, the soft-alkylating agents did not evoke morphogenetic JH effects,

A number of potential insect anti-hormones were tested in vivo as cytochrome P-450 inhibitors. The results contribute to the understanding of the mode of action of insect anti-hormones and help the design of further active compounds (see Appendices 2.1.9., 2.1.10., 2.2.6., 2.2.9.).

2/ Investment

Installation of the two new laboratory complexes resulted in a significant increase of research capacity and in bringing the

research methods used to an up-to-date level.

a) While the facilities of the old laboratories enabled mainly the synthesis of traditional type pesticides - including also insecticides -, the new organic chemistry laboratories are suitable for the synthesis of fourth generation insecticides, which require sophisticated preparative methods (see Appendix 4.).

b) Prior to the installation of the new biochemistry laboratory no biochemistry studies were possible . In that earlier situation only the biological activities of the synthesized compounds could be assessed, but it was not possible to investigate the mode of action of the compounds at biochemical level. Apart from scientific insufficiency of research work in general, the lack of biochemical investigation had deprived our research activity from rational design of chemicals to be based on biochemical knowledge.

In this respect the establishment of the biochemistry laboratory complex created a new situation. As the investigation of biochemical mode of action of the compounds became possible, the elucidation of the relationships between chemical structure and biological activity became more accessible, thus providing information for up-to-date biochemistry motivated design and synthesis of further compounds.

c) As a result of the installation of the nuclear magnetic resonance (NMR) spectroscope, the determination of the structure of the chemical compounds prepared under the project can be

carried out much more easily, compared to the former situation, where similar structure determinations were made on a contract basis requiring considerable waiting time.

d) The installation of the high performance liquid chromatograph (HPLC) permits the application of up-to-date separation techniques in biochemistry research, which is inevitably necessary for high standard biochemistry research.

These improved possibilities serve the realization of the immediate objectives. In the long run the new laboratory complexes and the instruments will serve also the development objective:: due to the versatility of their utilization they will be the basis of organic synthetic works within future research programs, included also UNDP/UNIDO project HUN/86/006 starting this year.

3/ Training

Three long term fellowship programs were completed (see Appendix 3.). Apart from their initial benefit, manifesting itself in serving the project's immediate objectives, these fellowships resulted in acquiring the highest standard of knowledge and skill in the relevant fields, thus creating a long term intellectual background for future research activity.

D/ Findings and lessons learnt.

1/ Research and development

By the development of two new types of selective anti-insect agents belonging to the category of juvenile hormone analoques (Appendix 1.1.), the possibility for their practical application in different fields of plant protection and sanitary insect control has been opened up. According to biological results obtained hitherto the potential fields of application are: insect control in orchards, control of scale insects, fly and mosquito control. Continued biological investigation may open up additional fields of application.

By the discovery of the highly active benzoyl-biuret type new insect chitin synthesis inhibitors a new class of anti-insect agents has been introduced for further optimization (Appendix 1.6.).

2/ Investment

See: C.2.

3/ Training

See: C.3.

E/ Recommendations.

1/ Research and development

Part of the results achieved within the project justify practical development, namely steps to be undertaken in order to introduce the chemicals into plant protection and sanitary practice. These activities are subject of a subsequent Project HUN/86/006 "Practical development of non-toxic anti-insect agents". Major part of the activities to be carried out by the above mentioned project concentrates on utilization of the objectives of the current project.

At the same time continued research on finding new selective anti-insect agents has to be carried out. This research activity, however, should be basically different from that of the current project, as findings obtained within the current project provides substantial theoretical background to be extensively utilized in future research.

Budapest, September 27, 1986.

Prof. Dr. Zoltán Király
director

Prof. Dr. Georg Matolcsy
project manager

F/ Appendices.

Appendix 1.

Compounds prepared and assayed for their biological activity during the project.

The compounds synthesized during the project for various biological activities (see below) were assayed either by our biologists and entomologists at the Department of Zoology or by subcontractors abroad or in Hungary. The details of the tests and the results can be found in relevant reports and publications. Some of the compounds were assayed in more than one test.

1.1./ Anti-juvenile hormone activity (vinylbenzenes, cinnamic acid derivatives, phenol and benzaldehyde derivatives and 1,1-dichloropropanol esters)	43 compounds
1.2./ Anti-ecdysone activity	10 compounds
1.3./ Chemosterilant activity (benzodioxoles, cyclic amino and hydrazino compounds, phosphor-containing compounds, chloromethyl esters)	52 compounds

1.4./ Mixed function oxidase inhibitors (methylenedioxybenzenes, cyclopropylamine derivatives, metyrapone derivatives)	15 compounds
1.5./ Pyrethroids (phosphor-containing analogues, sulfur-containing-analogues)	15 compounds
1.6./ Chitin-synthesis inhibitors (proinsecticides of benzoylureas, benzoylbiurets and cinnamanilides)	62 compounds
1.7./ Inhibitors of cuticle formation and catecholamine biosynthesis (catecholamine derivatives, (di)-thiocarbamates, mathematical)	96 compounds
1.8./ Compounds acting on insect neurotransmission	5 compounds
1.9./ Anti-sclerotizing activity	31 compounds

Appendix 2.

List of publications on the results of the Project.

2.1. Papers

2.1.1./ Matolcsy, Gy.; Feyereisen, R.; Van Mellaert, H.; Pál, A.; Varjas, L.; Bélai, I.; and Kulcsár, P.: Molecular modifications of benzylphenol and benzyl-1,3-benzodioxole types of insect chemosterilants. Pestic. Sci. 1986, 17, 13 - 24.

2.1.2./ Sohár, P.; Pelczer, I.; Váczi, I.; Tombor, A.; Matolcsy, Gy.: Conformational analysis of N-acylbicyclooctanes. Magn. Reson. Chem. 1985, 23, 506-513.

2.1.3./ Pap, L.; Hegedüs, E.R.; Bauer, K.; Ujváry, I.; Matolcsy, Gy.: Rapid method for the evaluation of nerve conduction blocking compounds. Comp. Biochem. Physiol. Vol. C1986 (in press).

2.1.4./ Matolcsy, Gy.; Bauer, K.; Pál, A.; Ujváry, I.; Bélai, I.; Gerlei, A.; Kardos, M.; Sohár, P.; Pelczer, I.: Phosphaneoxides as intermediates in the synthesis of potentially bioactive compounds. Acta Chim. Hung. 1986 (in press).

2.1.5./ Ujváry, I.; Hiruma, K.; Riddiford, L.M.; Matolcsy, Gy.; Roseland, C.R.; Kramer, K.: Role of β-alanine in pupal coloration and sclerotization in the tobacco hornworm, Manduca sexta. The effect of (aminooxy)acetic and hydrazinoacetic acids on cuticle formation. Insect Biochem. 1986 (in press).

2.1.6./ Matolcsy, Gy.; Ujváry, I.; Riddiford, L.M.; Hiruma, K.: Alkylenebisisothiocyanates - Novel insect growth regulatory action. Z. Naturforsch. 1986 (in press).

2.1.7./ Bélai, I.; Darvas, B.; Matolcsy, Gy.: Synthesis of alkoxybenzenes and alkoxyvinylbenzenes and their chemosterilizing and toxic activity on Planococcus citri (Hom., Pseudococcidae). Agric. Biol. Chem. 1986 (in press).

2.1.8./ Matolcsy, Gy.; Bélai, I.; Feyereisen, R.; Ujváry, I.; Varjas, L.; Darvas, B.; Kulcsár, P.; Fónagy, A.: Juvenoids bearing additional biofunctional moiety. Insect Biochem. 1987 (manuscript submitted for publication).

2.1.9./ Darvas, B.; Fónagy, A.; Kulcsár, P.: Inhibitory effect of fenarimol and nuarimol of cytochrom P-450 activity in the different larval stages of Sarcophaga bullata

(Sarcophagidae). Aust. J. Zool. (in preparation).

2.1.10./ Darvas, B.; Kulcsár, F.; Matolcsy, Gy.; Bélai, I.: The inhibitory effect of the soft analogue of -phenyl-ß-triazolium-metyrapone on cytochrome P-450 activity during pupariation in Sarcophaga bullata (Dipt., Sarcophagidae). Ent. Exp. Appl. (in preparation).

2.2. Conference papers

2.2.1./ Ujváry, I.; Kis-Tamás, A.; Novák, L.: Synthesis of some insect sex pheromones from aleuritic acid. Poster presented at the ACS DPC II. Special Conference (Snowbird, June 24-29, 1984).

2.2.2./ Bordás, B.: Stepwise canonical correlation analysis: A new approach for the study of structural requirements of broad spectrum activity. In: "QSAR and Strategies in the Design of Bioactive Compounds." Proceedings of the Fifth European Symposium on Quantitative Structure-Activity Relationships Bad Segeberg 1984 (Ed. J.K. Seydel), p. 389-392, Verlag Chemie, Weinheim, 1985.

2.2.3./ Ujváry, I.; Hiruma, K.; Riddiford, L.M.; Matolcsy, Gy.; Varjas, L.; Darvas, B.; Roseland, C.R.: Novel effect of ß-alanine analogues on the coloration and sclerotization

of insect pupal cuticle. Poster (No. 2B-07) presented at the Sixth IUPAC International Congress of Pesticide Chemistry (Ottawa, August 10-15,1986).

2.2.4./ Matolcsy, G.; Ujváry, I.; Riddiford, L.M.; Hiruma, K.: Inhibition of spiracle- and crochet-formation by 1,3-bis-isothiocyanates. Paper (No. 3A-05) presented at the Sixth IUPAC Intentional Congress of Pesticide Chemistry (Ottawa, August 10-15, 1986).

2.2.5./ Bordás, B.; DeMilo, A.B.; Haught, S.B.; Flippen-Anderson, J.: Some new insect moult inhibitors derived from benzoylbiurets. Paper (AGRO-4)) presented at the 192th American Chemical Society National Meeting (Annaheim, September 7-12, 1986).

2.2.6./ Fónagy, A.; Darvas, B.; Kulcsár, P.: Inhibition of the cytochrome P-450 dependent monooxygenases by fenarimol and nuarimol in different larval stages of Sarcophaga bullata (Sacophagidae). In: B. Darvas and L. Papp (eds.) Abs. First Int. Cong. Dipterology, Univ. Vet. Sci. Press, Budapest, 74., 1986.

2.2.7./ Darvas, B.; Kulcsár, P.; Bélai, I.; Matolcsy, Gy.: Soft analogue of α-phenyl-ß-triazolium-metyrapone as an in vivo inhibitor of ecdysterone biosynthesis on Sarcophaga

bullata. In: B. Darvas and L. Papp (eds.) Abs. First Int. Cong.

2.2.8./ Varjas, L.; Darvas, B.; Ujváry, I.: Induction of cuticular melanization in puparia of Sarcophaga bullata with ß-alanine analogues. In: B. Darvas and L. Papp (eds.) Abs. First Int. Cong. Dipterology, Univ. Vet. Sci. Press, Budapest, 245., 1986.

2.2.9./ Kulcsár, P.; Darvas, B.; Fónagy, A.: The effects of fenarimol and nuarimol, inhibitors of Cytochrom P-450, on the development and reproduction of Sarcophaga bullata. Abs. Sixth Int. Cong. Pesticide Chem., Ottawa, 3A-06, 1986.

2.2.10./ Matolcsy, G.; Bélai, I.; Ujváry, I.; Feyereisen, R.; Varjas, L.; Darvas, B.; Kulcsár, P.; Fónagy, A.: Juvencids bearing additional biofunctional moiety. Abs. Fourth Int. Symp. Juvenile Hormones, Niagara-on-the - lake, Ontario, 30., 1986.

2.3. Patent application

2.3.1./ Ujváry, I.; Matolcsy, Gy.; Bélai, I.; Varjas, L.; Darvas, B.: Novel insecticidal carbamate derivatives. Hung. Patent Application 4927/85 (1985).

Appendix 3.

3.1. Long term fellowship programs.

3.1.1/ Dr. Iván Bélai

Instituto de Quimica Bio-organica (C.S.I.C.)

Barcelona. Spain.

November 1983. - August 1984.

3.1.2/ Dr. Iván Bélai

Department of Medicinal Chemistry, College of Pharmacy,

Hillis Miller Health Center,

University of Florida, Gainesville, USA.

February 1986.- February 1987.

3.1.3/ Dr. Barna Bordás

United States Department of Agriculture,

Agricultural Research Service,

Beltsville Agricultural Research Center,

Insect Reproduction Laboratory,

Beltsville, Maryland, 20705, USA.

April 1985. - February 1986.

3.1.4/ Dr. István Ujváry

College of Forest Resources and Department of Zoology,

University of Washington, Seattle, USA.

January 1984. - November 1984.

3.2. Study tours

Prof. Dr. G. Matolcsy (1982): Oregon State Univ., Dept. of Entomol., Cornvallis, Oregon, USA; New York State Agric. Exp. Sta. Cornell Univ., Dept. Entomol., Geneva, USA; Agric Res. Sci. and Ed. Administr., Dept. of Agric., Beltsville, Maryland, USA; Univ. of Washington, Dept. of Zool., Seattle, USA; Zoecon Corp. Palo Alto, California, USA; Univ. of Toronto, Dept. of Zool., Toronto, Canada; Zool. Inst. Leuven, Belgium; Instituto Quimica Bio Organica, Barcelona, Spain.

Prof. Dr. G. Matolcsy (1983): UNESCO-UNEP-UNIDO, International Conference on Environmental Hazards of Agrochemicals in Developing Countries, Alexandria, Egypt; Institute of Org. Chem. Polish Academy of Sciences, Warsaw, Poland; Institute of Tropical Diseases, Gdansk, Poland.

Dr. L. Varjas (1983): International Symposium on Invertebrate Hormones, Strasbourg, France.

P. Kulcsár (1983): Ecole Normale Superieure, Laboratoire de Zoologie, Paris, France; Bernard Manchamp Laboratoire de Phytopharmacie INRA, Versailles, France.

Prof. Dr. G. Matolcsy (1984): Institut National du Recherche Agronomique, Versailles, France; Dept. of Zoology, Univ. of Washington, Seattle, USA; Division of Toxicology and Physiology, Dept. of Entomology, Univ. of California, California, USA; Institute for Comparative Environmental Toxicology, Cornell

Univ., Ithaca, USA; College of Pharmacy, Univ of Florida, Gainesville, Florida, USA.

Dr. B. Darvas (1984): XVII. International Congress of Entomology' 84, Hamburg, W. Germany; Agricultural and Research Council, Insect Chemistry and Physiology Group, Univ. of Sussex, Brighton, England.

Dr. B. Bordás (1984): 5th European Symposium on Quantitative Structure-Activity Relationships, Bad-Segeberg, W. Germany.

P. Kulcsár (1984): Laboratoire de Cytophysiology des Atnropodes, Univ. Pierre et Marie Curie, Paris, France; XVII. International Congress of Entomology' 84, Hamburg, W. Germany.

Dr. L. Varjas (1984): Laboratory of Entomology, Agric. Univ., Wageningen, Holland; Zoological Institute, Catholic Univ., Leuven, Belgium.

Prof. Dr. G. Matolcsy (1985): Dept. of Entomology, Univ. of California, Riverside, USA; Univ. of Arizona, Dept. of Entomology, Tucson, USA; College of Pharmacy, Univ. of Florida, Gainesville, USA; Dept. of Entomology, Purdue Univ., West Lafayette, USA; Dept. of Chemistry, State Univ., New York at Stony Brook, Stony Brook, N.Y., USA;

Dr. L. Varjas (1985): Dept. of Biology, Kanazawa Univ., Kanazawa, Japan; Dept. of Agric. Chem., Kyushu Univ., Fukuoka, Japan; Dept. of Medical Entomology, Nat. Inst. of Health, Tokyo, Japan; Nihon Nohyaku, Co. Ltd., Tokyo, Japan; Biological Institute, Nagoya Univ., Nagoya, Japan; Dept. of Agric. Chem., Kyoto Univ., Kyoto, Japan.

Prof. Dr. G. Matolcsy (1986): (preparation in progress) Purdue Univ. Dept. of Entomology, West Lafayette, Indiana, USA; College of Pharmacy, J. Hillis Miller Health Center, Gainesville, Florida, USA; Department of Pharm. Chemistry, School of Pharmacy and Liver Center, Univ. of California, San Francisco, USA; WHO, Geneva, Switzerland; CIBA-GEIGY AG, Basel, Switzerland.

Dr. L. Varjas (1986): Fourth International Symposium on Juvenile Hormones Physiology, Biochemistry and Chemistry, Niagara-on-the-Lake, Canada.

Dr. Ujváry (1986): Department of Chemistry, State Univ. of New York at Stony Brook, N.Y., USA; Sixth International Congress on Pesticide Chemistry, Ottawa, Canada.

Appendix 4.

4.1. New laboratory equipment (covered by UNDP)

2 CAMAG UNIVERSAL UV LAMP + ACCESSORIES

1 ROTARY EVAPORATOR R-110/A 10955

2 METTLER ELECTRONIC PRECISION BALANCE PE 1600

1 BÜCHI ROTAVAPOR WITH ACCESSORIES EL-130/S

6 MAGNETIC STIRRER RCT. INCL. STIRRING BAR STANDARD F37120

4 MAGNETIC STIRRER RET. INCL. 40mm LONG 7 mm DIA

3 FLASH CHROMATOGRAPHY COLUMN KIT 7022-2 (JANSEN)

3 SOLVENT RESERVOIR 500 ml 7092-4

2 HPLC PUMPS 110A (BECKMAN)

1 GRADIENT ORGANIZER MODEL 340

1 DETECTOR UV/VIS MODEL 160

1 CONTROLLER MODEL 420

1 MODEL CR3A SINGLE CHANNEL INTEGR. RECORDER

1 STRATER KIT

1 ULTRA-TURRAX DRIVE T 18/10 COMPLETE WITH ACCESSORIES (BECKER)

10 IKA STIRRING MOTORS + ACCESSORIES

1 SARTORIUS ANALYTICAL BALANCE

CHEMICALS

4.2. New laboratory equipment (covered by the government)

Furniture of the new biochemistry- and organic chemistry units

HP-41 C type programmable calculator with accessories

Commodore C64 type computer with peripherals (color monitor, printer and floppy disk drive)

OP 211 digital pH measuring equipment

Anaerob thermostat

Ultrathermostat

Ministat

Laminar-box

Laboratory hoods

OWA labor balance

Microscope with accessories (ZEISS, type Laboval 4.)

Vacuum drying boxes

Infralamps

Boetius melting point equipment

Automatic sample collectors

Chemicals

Appendix 5.

5.1. Foreign subcontractors:

5.1.1. Dr. Lynn M. Riddiford

College of Forest Resources and Department of Zoology,

University of Washington, Seattle, USA.

5.1.2. Dr. R. Feyereisen

Department of Entomology

Oregon State University

Corvallis, Oregon 97331, USA.

5.2. Domestic subcontractors:

5.2.1. Dr. I. Kiss

Nehézvegyipari Kutató Intézet

1983 Veszprém, Hungary.

5.2.2. Dr. H.E. Randványiné

CHINOIN Gyógyszer és Vegyészeti Termékek Gyára

1045 Budapest, Tó u. 1/5.

5.2.3. Eötvös Lóránd University of Sciences and Arts,

Department of Organic Chemistry,

1088 Budapest, Múzeum krt. 6/8.

Appendix 6.

6.1. Government project professional personnel:

Prof. Dr. G. Matolcsy project manager

Staff members:

Dr. Iván Bélai

Dr. Barna Bordás

Dr Béla Darvas

Mrs. Anikó Gerlei project secretary and research worker

Mrs. Anikó Kenessey

Mr. Péter Kulcsár

Mrs. Krisztina Pelejtei

Mr. András Székács

Dr. István Ujváry

Dr. László Varjas

6.2. Internationally recruited project professional personnel:

Yassin Darwish

Duong Anh Tuan