

DEC 1976

SCIENCE BULLETIN

National Science Council
2 Canton Street
Taipei, Republic of China

NSC Finances Chemical Research

Recognizing the important role played by allied chemical industries in the national economy (contributing to 20 per cent of the GNP), the National Council has been allocating more funds for chemical research in the past year and a half. To obtain short-term as well as long-term benefits of R/D activities, NSC will (a) support creative basic research, (b) help universities build up brain power and R/D facilities in support of local industrial growth, and (c) coordinate or undertake industrial research activities.

For the last two years, research priorities have been assigned to (1) effective utilization of natural gas, (2) advancement of polymer science and technology, (3) synthesis of pharmaceutical drugs, (4) search for new protein sources, and (5) synthesis of industrial intermediates or fine chemicals including the isolation and uses of the local natural resources.

Providing specific definitions of research purpose and setting-up a research priority for the local chemical research community represent a new challenge to researchers and administrators. It is hoped that these efforts would make the research activities more effective and responding to societal needs. To make this reorientation, NSC has had its share of difficulty. However, through discussion and persuasion, NSC has opened up dialogue between researchers and administrators and has seen gradual increase in the numbers of solicited research projects and reorientation of research effort as shown in Table. I.

In general, random collection of scientific or technological data by an individual scientist or engineer is discouraged. NSC encourages, instead, group research and systematic collection of scientific knowledge by a critical mass of scientists. NSC strongly emphasizes desirability of concluding

research with clear implication for future application in meaningful theoretical or applied works. For technological research, NSC hopes that the research would facilitate or eventually lead to industrial application.

To strengthen reviewing process for research proposal, NSC has set up a review system requiring at least two reviewers, for each proposal. This brought about 10 to 20 per cent rejection of research proposals submitted to the Council.

The reviewers are selected to accomplish following purposes, (1) evaluation of the merit and the soundness of proposal, (2) gathering of relevant information from the senior scientists (3) coordination of mutual research activities among the concerned parties, and (4) education of junior scientists, by sending them "good" research proposals for study.

The first purpose is a MUST; the second purpose is pursued often when an appropriate reviewer is believed to have an easy access to a large quantity of valuable information. The last two purposes are pursued only when the Council is certain of the proposal and the outcome of further reviewing process is not critical. It is felt that Chinese scientists tend to be reserved and non-participating; this is particularly so in an open discussion. It is hoped that pursuit of the last two purposes would facilitate mutual understanding among local scientists.

After the review process is over, the proposal is granted when NSC needs (1) a man in a particular field to establish a foundation, (2) a particular work to be started or (3) a relatively short-term result from the project. The difference between the first two criteria is a matter of emphasis and expectation of the quality of worker or his work.

After a project is contracted,

monitor work is done by a formal report at the end of the project contract and by the informal progress reports or discussion between the scientists and the Council. It has been found that the informal progress report or discussion tends to be more fruitful; it provides opportunity to both sides to understand each other's position and provides timely modification of the research course.

Major research activities in the chemical science and technology are divided into the following.

(1) *Utilization of natural products.* In this section NSC has granted 14 projects (NT\$3,705,000 or US\$98,000) to nine investigators in the fiscal years of 1976 and 1977.

Most of them are involved in the Chinese herbal researches. Professor F. C. Chen of National Taiwan University isolated Rhusflavonance, mp 204-206°C. and a new Rhusflavone, $C_{30}H_{20}O_{10}$, in addition to hinokiflavone, ametoflavone, agathisflavone and robustaflavone from the seed kernels of *Rhus succedanea*, *Anacardiaceae*. Professor C. M. Chen of National Tsing-Hua University obtained Angioside $C_{12}H_{18}O_{18}$, and several phytosterol and three glucosides from the rhizomes of *Angiopteris lygodiiifolia* and *Cibotium barometz*. Also studied was the fern constituents of *Selaginella tamariscina*. Screening tests for biological activities of three Chinese herbs as guidance at the beginning of study or as follow-up study are unfortunately less emphasized and remained to be corrected.

In the essential oil field, the emphasis is on the economic value of the oil. Thus, using gas chromatography, Professor Y.T. Lin of NTU has succeeded in finding several camphor

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Lipid Intakes and Incidence of Atherosclerotic Cardiovascular Diseases in Taiwan

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It has been generally accepted that higher serum cholesterol level is positively correlated with higher risk of developing coronary heart disease (CHD), not only in populations with a high prevalence of CHD as in the U.S.A. but also in Japan where CHD is much less common.

It is also well known that CHD is multi-factorial. The related factors include Hypertention, obesity, inactivity, cigarette smoking and hypercholesterolemia etc.

It has been generally accepted that dietary saturated fatty acids and

cholesterol play an essential role in the etiology of hypercholesterolemia, and thus lead to atherosclerosis particularly arteriosclerotic heart disease, namely coronary heart disease.

Recently however, Wen and Ger-shoff (1) of Harvard School of Public Health reported that the dietary lipid increases in the post-war period could, at best, account for only 24 per cent of the actual increase in the mortality of CHD.

In Taiwan the mortality rate or prevalence of arteriosclerotic heart disease is still quite low if compared with those of U.S. and Canada. However, the mortality has been increasing during the past 20 years (Fig. 1). At the same time, dietary lipids and other nutrient intakes have also been in-

creasing considerably.

The object of this paper is: to examine to what extent the increase in dietary lipids is correlated to the increase in CHD mortality rate.

The dietary changes which occurred during the past two decades are as follows. The nutrients and calorie intakes were calculated from the Taiwan Food Balance Sheets prepared by the Joint Commission for Rural Reconstruction. These data are the availabilities of nutrients. They are known to be higher than the actual intakes, however, because the method used in preparing the Food Balance Sheets did not change much during the period, data are comparable to each other and the trend of dietary changes can be recognized (Fig. 2, 3).

Available calories per capita per day increased from 2056 kcal in 1950 to 2697 kcal in 1972, an increase of 31 per cent. Total fat availability increased from mere 27.9 g to 68.8 g, a dramatic increase of 146 per cent during the same 22-year post-war period. If expressed as % of the total calories, the increase of total available fat is from 12.2 per cent in 1950 to 22.9 per cent. Intake of saturated fatty acids increased from 3.3 per cent to 6.1 per cent of the total calories, to the intake of polyunsaturated fatty acids also increased from 2.3 per cent to 5.8 per cent of the total calories, and thus the P/S ratio (ratio of polyunsaturated to saturated fatty acids) increased from 0.68 to 0.92. This was fortunate because it means relative decrease in saturated fat intake which is considered to play an essential role in causing hypercholesterolemia. Cholesterol intake was only 78 mg in 1950 but increased to 217 mg in 1972.

From above mentioned lipid intake data one can calculate the possible change in serum cholesterol level during the decades according to the following formulae developed by Hegsted et al. (2) and Keys et al. (3). Cholesterol $A = 2.16 (S) - 16.5 (P) + 6.77 (C) - 0.5 \dots$ Hegsted et al. Cholesterol $B = 1.35 (2 S - P) + 1.5 (Z) \dots$ Keys et al.

Table 1 shows such calculations of possible changes in serum cholesterol between 1952 or 1956 and 1970

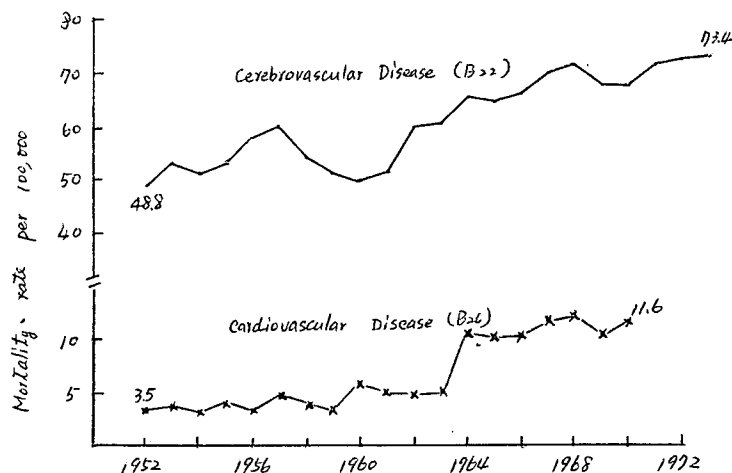


Fig. 1. Trend of mortality rate of cardiovascular and cerebrovascular disease.

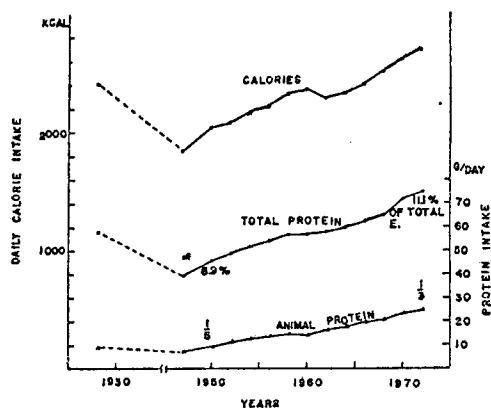


Fig. 2. Trend of calorie and protein intake.

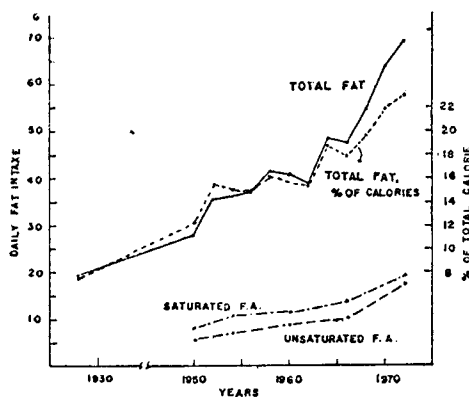


Fig. 3. Trend of fat intake.

or 1972. The estimated changes are not so large, ranged between 3.4 and 6.1 mg/100 ml serum (Table 1).

Truett and his coworkers (4) developed a formula for calculating probability of risk from developing coronary heart disease in 12 years for 50 to 62 years old men using serum cholesterol and other data. We have calculated such a probability for a 55 years old men assuming serum cholesterol level is the only variable and other factors remained unchanged.

For a 55 years old man P of risk from suffering CHD increased only 4.4 per cent between 1956 to 1970 because of the change in dietary lipid, intakes. On the other hand the actual increase in CHD mortality was 41.6 per cent. Therefore, the contribution of dietary lipidly factor through serum cholesterol increase in CHD mortality increase was only 10.6 per cent. This result suggest that combination of other factors such as stressful life pattern, inactivity, hypertension relative body weight and cigarette smoking etc. may be much more important than the dietary lipids alone in causing CHD. (Table 2).

According to Tseng et al. (5), the age adjusted prevalence of CHD is much higher in Taipei, an urban area, than in San-Chih, a rural district. The ratio found was about 5 to 1 with male and female combined. However, the incidence of hypercholesterolemia was only slightly higher in urban Taipei, whereas serum TG and lipoproteins were much higher in Taipei than in San-Chih (Table 3).

Dietary survey of rural San-Chih: In order to compare further the difference between urban Taipei and rural San-Chih we have conducted a dietary survey in the rural San-Chih. The method employed was a 5-day weighing method, and the results are presented below. It was interesting to find people, who were mostly farmers and their family, using lard instead of vegetable oils in cooking. This was in contrast to Taipei where people are mostly using vegetable oils in cooking. However the rural people eat much less pork than Taipei citizens, therefore, their dietary P/S ratio was actually not much different from that of Taipei citizens. (Table 3). The total fat intake was less than that of Taipei, and this might be somewhat related to the difference in CHD prevalence between Taipei and San-Chih.

References

1. Wen, C.P. and S.N. Gershoff, Am. J. Cl. Nutr. 26: 616, 1973.
2. Hegsted, D.M. et al., Am. J. Clin. Nutr., 17: 281, 1965.
3. Keys, A. et al., Met ab. Clin Exptl. 14: 747, 1965.
4. Truett, J. et al., J. Chronic Disease 20: 511, 1967.
5. Tseng, W.P, Report to NHA, 1975.

Table 1
Estimates of changes in serum cholesterol associated with changes in dietary lipid consumption

| Period | CholA mg/100 ml | CholB mg/100 ml |
|-------------|--------------------|--------------------|
| 1956 - 1970 | +5.35* | +3.41 |
| 1956 - 1972 | +6.08 | +4.20 |
| 1952 - 1970 | +5.51* | +3.30 |
| 1952 - 1972 | +6.74 | +4.09 |

*Used for estimating the serum cholesterol levels in 1956 and 1952.

Table 2
Estimated probability of risk for a 55- or 65-year old Chinese male from developing CHD in 12 years

| Year | P | Increase in P Period % of increase | Actual increase in mortality % | Contribution of dietary factors in CHD mortality increase % |
|--------------------|--------|---------------------------------------|--------------------------------------|---|
| 55-year old | | | | |
| 1952 | 0.1172 | | | |
| 1956 | 0.1173 | 1956-70 4.4 | 41.6 | 10.6 |
| 1970 | 0.1224 | | | |
| 65-year old | | | | |
| 1952 | 0.2149 | | | |
| 1956 | 0.2152 | 1956-70 3.9 | 137.7 | 2.8 |
| 1970 | 0.2235 | | | |

Estimated serum cholesterol levels:

1952: 169.0 mg %, 1956: 169.2 mg %, 1970: 174.5 mg %.

Table 3
Comparison of age adjusted prevalence and related factors of coronary heart disease between urban and rural areas in Taiwan (1973-74)

| | Urban (Taipei) | Rural (San-Chih) |
|-----------------------------------|-------------------|---------------------|
| | % | % |
| Prevalence of CHD | 2.7 | 0.5 |
| Hypertension (160 mmHg, systolic) | 23.8 | 20.5 |
| Hypercholesterolemia (250 mg %) | 5.5 | 4.3 |
| Hypertriglyceridemia (200 mg %) | 13.5 | 7.7 |
| Type IIa lipoproteinemia | 6.3 | 2.5 |
| Type IV lipoproteinemia | 22.9 | 13.4 |
| Dietary lipids | | |
| Total fat, % of total kcal | 22.8 (64.1g) | 17.5 (46.2g) |
| Saturated f. a., % of total kcal | 6.34 | 6.01 |
| Polyunsat. f. a., % of total kcal | 4.39 | 3.97 |
| P/S ratio | 0.69 | 0.66 |
| Cholestirol, mg/day | 391 | 265 |
| Physical exercise, points* | 4.9 | 8.0 |

* According to the criteria of Evans County study.

NSC Finances Chemical Research

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trees with extremely pure and high camphor content in the leaves. This is expected to revolutionize production methods of the natural camphor. In addition to the continuous search for better variety, cultivation work by grafting and finding of new production method are to be started in this fiscal year.

Miss S.M. Chang of Academia Sinica investigated the effect of synthetic media on the growth and the nutritional value of Lemnaceae. From four species, *Lemna paucicostata*, *Wolffia arrhiza*, *Spirodela polyrrhiza* and *Spirodela sp.*, their protein and starch content are found to be as high as 16 to 40 and 18 to 24% (dry mass) respectively. NSC's interest in this project is to find out the possibility of large-scale production of lemanaceae for the poultry feed, chemicals or industrial starch source.

In the near future, NSC will also look into the utilization of local essential oils for perfumery raw materials.

(II) *Organic synthesis.* All together NSC has granted NT\$2,830,000 (or US\$74,000) to seven investigators. Most of these researches involve syntheses of heterocyclic compounds and organosilicon compounds with potential uses in medicine or agriculture.

Professor C.T. Chen of Academia Sinica is interesting in the syntheses of pyridine derivatives as potential antitumor agents. Dr. Y.S. Kuo of NTU is working on the syntheses of Rannunculin for antileukemia agent. The compound contains a S-formed aglycone and can be isolated from *Ranunculus acris* L. *R. Cordiophyllus hook* and *Anemone Patens* L. *van Wolfgangiana*. In a separate study, Dr. Y.C. Lin of the Medical School of NTU has found that Cordacin which was isolated from the local *Drymaria Cordata* (L) Willd has high antileukemia activity with low toxicity. The two compounds are almost identical in their structures with Cordacin having R and S-formed aglycone. In this study, furfuryl alcohols derivatives would be used as starting materials.

Professor S.L. Liu of NTU in his first year project has synthesized $X-C_2H_4Si(OR)_3$. In addition to the syntheses of more organosilicon compounds, such as $X-C_2H_4Si(NR)_3$, $X-C_2$

$H_4Si(SR)_3$ and $R_2Si(OR)_2$, these compounds would be tested for their efficacy on the growth of rice. According to patents disclosures, certain type of organosilicon compounds facilitate growth and increase yield of wheat and corn; however, their effect on rice has not been tested.

(III) *Organic reactions.* Of thirteen projects (NT\$2,095,000 or US\$55,000) under this category, six are photochemical reactions. Professor C.T. Yeh of THU reported a rate constant of $K=1.5 \times 10^{14}$ cc/mole, sec for the reaction of hydrogen radical and methyl radical at 56°C. and 300 Torr pressure. The radical was generated by the triplet mercury photosensitized decomposition of ethane. Using diazomethane as the methylene source, Professor S.Y. Ho of THU reported the reaction of singlet methylene with ammonia to form methylamine in excited state as reaction intermediate.

Professor K.T. Liu of NTU in his attempt to study steric effect of 1-methyl group of norbornyl system, has undertaken SN2 reaction of norbornyl derivatives with sodium thiophenolate and concluded the existence of steric hindrance of the 1-methyl group on the reactivity of C-2. The magnitude of this steric hindrance depends upon the nature of reactions. In THU, Professor C.H. Liu has generated SiF2 via disproportionation of SiF4 with Si. This active intermediate is to be tested for its ability to add onto inorganic multiple valence such as $C \equiv N$ or $>P=N$, $C \equiv O$ etc.

(IV) *Spectrometric study of molecular structure.* Altogether fifteen projects were granted during fiscal year 1976 and 1977. (NT\$2,473,000 or US\$65,000). Of 15 projects, nine projects have duration less than two years, and hence, are only in the initial period of installing instruments and

starting-up. Professor H. Chang of Tsing Hwa University in the last few years has been setting up a laser light scattering laboratory. Temperature dependence of light scattering by the one-magnon excitation in NiF2 crystals was studied. They found that temperature dependence of frequency and line width agrees with previous far infrared adsorption data. However, the temperature of the integrated intensity follows the theoretical prediction but deviates from the far infrared data. In the other studies, gaseous bromine and chlorine were selectively excited. Moreover, using an argon ion laser of 300mv at 5145Å, they have taken Raman spectra of dimeric chlorophyll to determine its symmetry.

(V) *Organometallic complexes and their use in analytical chemistry.* Altogether there are eleven projects being granted in this period (NT\$1,550,000 or US\$40,800). Professor T.M. Hsu of National Taiwan University investigates thermodynamic and spectrophotometric properties of copper-ferrocene complex. In the field of metal complexes of macrocyclic ligands, Professor P.Y. Sun of NTU will prepare rare earth metal complexes of phthalocyanine from various sources including hydrogen phthalocyanine (PCH₂); Professor C.S. Chung of Tsing Hwa University prepares copper(II) complexes of tetra-amine macrocyclic compounds.

Professor H.S. Cheng of Tsing Hwa University is interesting in the complex formation of tin ion and aspartic acid; the complex salt will be characterized and compared with possible tin complex in the can solution of asparagus. Professor Y.M. Chen of NTU studies continuous separation of major components in Monazite by electrodialytic ion exchange membrane.

Table 1
Chemical R/D Under NSC

| Nature: | \$ (# of projects) | | |
|-------------|---------------------|-------------|-------------|
| | 1975 | 1976 | 1977* |
| Science: | 160,000(39) | 207,000(44) | 182,000(35) |
| Basic: | 141,000(36) | 167,000(38) | 126,000(29) |
| Applied: | 19,000(3) | 40,000(6) | 56,000(6) |
| Technology: | 140,000(15) | 155,000(24) | 115,000(14) |
| Basic: | 40,000(8) | 80,000(15) | 36,000(7) |
| Applied: | 100,000(7) | 750,000(9) | 79,000(7) |

*Up to Aug. 1977.

(To be continue in next issue)