Problems of Quality Control in Homoeopathic Drugs

—Dr. J. N. Tayal
Ex-Director CIPL, Ghaziabad

Dr. T. M Cook* of Nelsons, gave a talk on the problems of *Quality Control in Homoeopathic Drugs* at the seminar on problems of Homoeopathic potentization at the Royal Homoeopathic Hospital, London on 14 October, 1978.

During the course of his talk, Dr. Cook emphasised that modern techniques and systems of quality control do not invalidate the classical procedures, Indeed they are enhanced. According to Dr. Cook, if modern advances in scientific and medical knowledge had been available to Hahnemann he would certainly have taken advantage of them. Hahnemann of all doctors, could never be accused of being reactionary.

An essential prerequisite of quality control is that personnel engaged in manufacture are adequately trained and experienced and their duties and responsibilities are clearly explained.

Also. high standards of personal cleanliness must be maintained by all personnel and hand washing facilities made available and used regularly. Protective clothing—including clean overalls and head dress be worn at all times in manufacturing areas, not only by manufacturing personnel, but also by the visitors, entering manufacturing premises. Separate changing rooms should be provided for this purpose. Stringent house keeping methods must be employed and floors regularly washed and all surfaces where dust and dirt may collect wiped out regularly. Utensils should be washed thoroughly each time after use. Naturally, smoking, drinking and eating are not permitted in manufacturing areas under any circumstances.

So far as our country (India) is concerned, the Drugs Act, and the Rules made thereunder (as ammended to date) stipulate requirements for premises and personnel engaged in the manufacture of Homoeopathic Drugs.

According to Dr. Cook, specimens may be dried and pressed for retention or photographed and, in certain circumstances, subject to micro-structure analysis from which microphotographs are taken. Release of all raw materials from the *Quarantine Stores* is made only on the authority of the person responsible for *quality control* and only after assuring that they are labelled *fit for use*. Rejected materials should be promptly destroyed. Labels for all the finished packed products are also subjected to *Quality Control Inspection* to ensure their accuracy and correctness before they are released to the production area.

Further stipulations narrated by Dr. Cook are :

(a) At commencement of each manufacturing step, all equipment is inspected to ensure that it is clean and free from contamination from any other raw material/(s) or product/(s). At each stage, all material and equipment are carefully labelled to identify the materials being processed and each discrete quantity of raw material or product is labelled with a batch number. Written manufacturing procedures are closely followed in each manufacturing step and batch records are completed indicating times, temperatures, weights etc.

★ Based on an article "Homoeopathic Potentization" published in the British Homoeopathic Journal, Vol. LXVIII No. 2, April 1979, Page 107.

Thus the history of each batch including the utilization of raw materials and even packing materials, may be checked.

(b) At any time during manufacture and packaging, quality control personnel are required to make spot checks and take *samples* for laboratory analysis, thus monitoring every operation. Particular care is taken in the preparation of *mother tinctures* and *potencies*, to ensure absolute purity and reproducibility.

(c) On completion of manufacture and packaging representative samples of the finished product are taken according to prescribed procedures and labelled with the batch number and identity. Analytical tests are carried out in the Laboratory to ensure that the product meets the finished product specification and then is the product finally released from quarantine to the store to await despatch.

Samples of each batch of finished product are always retained in the laboratory. Storage conditions are carefully controlled to ensure that the products do not deteriorate before being passed to the practitioner. Finally, all manufacturing records are checked and filled and all equipment utilized in the manufacture is cleaned in accordance with the cleaning schedules, which lay down cleaning and inspection operations for individual item of equipment.

It may be pointed out that in-process and finished product quality control specified by Dr. Cook as above for the United Kingdom is amply covered by the provisions of Drugs Act of India, which emphasises cleanliness and analysis for ensuring quality of the finished product as well as raw material during the different stages of manufacture as also after manufacture. According to Dr. Cook, general precautions for ensuring quality which apply to all manufacturing operations include : (i) segregation of processing areas to avoid possible cross contamination (ii) the use of laminar air-flow equipment or air-conditioning and all operations carried out in such a way that the risk of contamination is minimised. A recent innovation is micro-biological testing by swab or settle plate method to monitor environmental contamination of all manufacturing area. All these aspects are stipulated in the provisions of the Drugs Act to ensure freedom from cantamination in India.

Quality Control of Homocopathic Potencies :

According to Dr. Cook, quality control associated with homoeopathic potencies is an area which presents the greatest challenge to the Quality Analyst. We do not know or understand, yet alone measure the intrinsic forces or vibrations which may play a part in the healing process of homoeopathic potencies, make it almost impossible to apply analytical tests by conventional methods in the laboratory. Even a relatively low potency such as 6x, with concentrations of individual 'active ingredients' less than one part per million is outside the accuracy of many modern instruments. For this reason, only mother tinctures are subjected to a more comprehensive analysis, both qualitative and quantitative. Additionally, we have the problem of chemical complexity of the natural extract contained in the original mother tincutre. These may be inorganic or organic with complex mixtures, including minerals, amino acids, proteins, steroids, vitamins, organo-metallic compounds, alkaloids etc.

According to Dr. Cook, the conventional allopathic approach to quality control in manufacture is to place great reliance on the assay of the final product which usually incorporates one or two readily identifiable 'active ingredients' all of them at relatively high levels of concentration. Because of the complexity and the high dilution of homoeopathic remedies, this approach is not possible. Hence, it is considered advisable that in-process-quality control embracing every step of the preparation from raw material to finished products is critical in ensuring the purity and safety of homoeopathic medicines. Thus a system of quality control is even more vital in the manufacture of homoeopathic drugs than in

their allopathic counterparts. According to Dr. Cook, at Nelsons they have recently developed a device for developing electronically the presence of medicament in all homoeopathic pharmaceutical forms, tablets, granules, pilules, ointments etc. This represents a vital interest in quality control.

The test is very sensitive even on materials which have been especially dried on medication, and it enables us, therefore, to monitor any Homoeopathic medicine from any source. While commenting on the present methods employed and the progress made in identifying and examining the constitution of mother tinctures, Dr. Cook made the following observations :—

1. Physical Properties :

Mother tinctures and potencies may be tested routinely for their *physical properties, specific gravity, refractive index, colour* and *smell.*

2. General Tests :

These may include *dry residue* (total solids), pH, *water content* (Karl Fisher Technique) and *percentage alcohol content.*

3. Analysis of Chemical Elements :

These assays are carried out by conventional chemical methods and can provide a means of identification and guide to the purity of mother tinctures and even for low potencies. An example analysis of crataegus and Nux Vom ica is given below—

	Crataegus ϕ	Nux. Vomica ϕ
Iron, parts per million	1.9	0.3
Calcium, parts per million	1500	1.9
Sodium, parts per million	16.0	6.3
Sulphur, percent	0.003	0.005
Nitrogen, percent	0.005	0.005

(The above figures reveal great differences in the contents)

Other trace elements present in low concentration include zinc, potassium, copper, cobalt, selenium, and manganese. Also differences in assay occur between mother tinctures, prepared from plants growing in different localities.

Thin Layer Chromatography :

This technique is now widely used and shows characteristic bands on a layer of silica-gel of 25-250 thickness, each band representing a specific chemical constituent of the mother tincture. These bands constitute a 'thumb print' for not only each mother tincture itself but different batches of the same mother tincture. Various solvent systems have been used, such as, *butanol/acetic acid* or *methanol/choloro form* over development distance of about 10 cm. Comparison of British, French and German mother tinctures showed considerable variation in the composition of the soil in which the original plant specimen was grown.

5. Microcrystallography :

Dr. Cook further said that this technique was developed in the Nelson Laboratories and provides a spectacular illustration of the variety and complexity of the homoeopathic medicines. Tests are performed by making a balanced mixture of chromium and nickel salt solutions with the mother tincture of the plant. The mixture is then crystallised under controlled conditions of humidity and temperature and the resultant crystal pattern photographed under the microscope using a special filter system. The crystalisation pattern is characteristic of the particular mother tincture and provides a means of identification ; this technique is not feasible with liquid preparations. All the 5 analytical techniques set forth above are being freely employed in the Homoeopathic Pharmacopoeia Laboratory (Government of India) situated at Ghaziabad. Moreover, the sophisticated analytical procedures, including physico-chemical techniques, such as IR, UV, etc.) microbiological as well as pharmacological methods are under development at the above Laboratories under the guidance of the Director, Dr. P. N. Varma, with whom the analytical and quality control procedures have been discussed in detail. The physical, physico-chemical and pharmacognostical characters have been stipulated in detail in the Homoeopathic pharmacopoeia, which has so far covered several drugs. It is hoped that the Homoeopathic Pharma-

copoeia Laboratory is adequately equipped with men, materials and leadership to undertake routine analysis as well as research in quality control of Homoeopathic drugs manufactured in India. It is hoped that in course of time the team of scientists in the Laboratory will render yeomen service to the field of quality control and bring the quality of the manufactured drugs at par with that in other western countries. It is hoped that with the guidelines established by the Homoeopathic Pharmacopoeia Laboratory, standards for not only the Raw materials but also compositions will be worked out. This will be a great landmark in the field of Drug standardisation concerning Homoeopathic Drugs.

ABSTRACTS

A. 1. Clinical Research in Homoeopathy, its Scope, Venues and Methodology : Kaur, Gulraj & Singh V.P.; Homoeopathic Caravan, 1979, 1(2). According to the authors, requisites of Clinical Research are : —

(a) Motive for Research,

(b) Hypothesis

(c) Personnel

Elaborating, Motive for Research the authors have mentioned that behind every research there is a spiritual, "Quest of the unknown". One who desires to conduct research must have a burning desire for knowledge which can be used as a means of elimination of (or to minimise) the suffering of mankind. This should be the sole motive. Regarding. hypothesis, the authors conclude that in Homoeopathy drug pathogenesis' are the hypothesis' which are subjected to test or confirmation in Clinical research. Regarding the personnel, it has been emphasised that a good research worker should have the qualities of : (i) sense of responsibility, (ii) sound intellect (iii) ability to interpret results so as to distinguish between the right and the wrong, and (iv) absolute freedom of the mind. Research methodology has been divided into (a) Material-subject patients and drugs, (b) Stardardised case taking and Repertorisation, (c) Observation and Data Collection, (d) Data analysis and conclusion, and (e) Communication. Under each head, the authors have emphasised clarity of thought, precision in action and complete as well as prompt reporting to the profession.

A. 2. A Study of Essential oil of Oenanthe Stolonifera (Wall) : Arvind Geda. R. K. Thappa and M. M. Bekadia, Indian J. Pharm. Sci. *Vol. 41*., No. 6., 1979 ; 223. *Oenanthe Stolonifera* (*Wall*) (Syn. *O. Javanica*) is an aromatic plant belonging to the family Umbelliferae. It is a perennial stoliniferae herb found in marshy place and on river banks in North India from Kashmir to Assam. In Madhya Pradesh it occurs as a weed in the croplands at river bank. In Malwa region it is known as *Ghora Ajawan.* The authors obtained essential oil from the plant by steam distillation of the flowering top in an yield of 1.72%. A systematic study revealed that volatile oil mainly consisted of dillapiole, β-phellandrene, β-caryopyllene, caryophyllene oxide, α-pinene along with a number of other minor constituents. The significance of the work is that dillapiole is a minor constituent, while phellandrene reported by previous workers as a major constituent is present as a minor one only.

A. 3. Evaluation of Essential Oil from Leaves of Adhatoda Vasica as an airway smooth muscle relaxant : J.L. D'cruz, A.Y. Nimbkar, and C.K. Kekate ; Indian J. Pharm. Sci. *Vol. 41* No. 6, (1979). The leaves of *A. Vasica* on hydro-distillation yielded 0.03% V/W of essential oil. The authors studied the activity of the oil on guinea-pig tracheal chain preparation. The authors also determined its influence on the responses elicited by two alkaloids, occuring in the crude drug, viz. *Vasicinone* and *Vasicine* and on ephedrine induced relaxations. The oil is shown to possess *bronchodilator* as well as vasicinone and vasicine potentiating activity.

A. 4. Studies on the Anti-fertility Properties of Embelia Ribes-I, Embelin : M. Krishnaswamy and K. K. Purushottaman ; Indian J. Pharm. Sci. *Vol. 41*, No. 6 ; (1979) Embilin (2, 5 dyhydroxy-3 Undecyl (1:4 benzoquinone) isolated from the seeds of *Embelia ribes* (Myristinaceae) was studied for its antifertility activity at 100 mg.

and 50 mg per kg. body weight. The drug shows innibition of parturition to the extent of 87.5 and 61 percent respectively at 100 mg. and 50 mg. per kg body weight, thus proving that *Embelin* is the active principle contributing to the antifertility activity of E. ribes. Regarding the oestrogenic and antioestrogenic activity of the drug it was observed that Embelin at the dose level of 100 mg. per kg. body weight does not increase or decrease any of the oestrogen sensitive parameters, such as uterine protein, glycogen, alkaline phosphate. Uterine weight also remains unaltered. The authors conclude that the drug has no oestrogenic or antioestrogenic action. (The readers may rlso refer to page 13 of the September, 1979 issue of the Bulletin on Embelia ribes, where biological activity of the extract and active principle of Embelin has been mentioned).

A. 5. Pharmacognosy of Arctium Lappa Linn root, A possible adulterant of Kuth-A preliminary study : H.C. Pandey and H.P. Sharma ; Indian J. Pharm. Sci. *Vol. 41* No. 6 (1979) *Arctium Lappa Linn* (fam. Compositae) a tall herb with carrot like roots having pungent aromatic taste and camphoraceous odour occurs in the Western Himalayas at an altitude of 1900 to 3200 M. The dried roots of the plant show close resemblance to market samples of "Kuth" in taste, odour and fracture. The paper deals with comparative pharmacognostic studies of A. Lappa roots and those of the commercial samples of "Kuth."

A. 6. Pharmacognostic Studies of Acorus Calamus and its Adulterants : D. Dey and M. N. Das ; Indian J. Pharm. Sci., *Vol. 41*, No. 6. (1979) *Acorus Calamus* has been used as emetic, expectorant, antispasmodic and nervine sedative in the Indian system of medicine since ancient times. This drug alongwith its adulterants *Alpinia galanga* and *A. offinarum* is available in the market under the name 'Vach'. The authors have reported detailed pharmacognostic studies with the object of checking the adulteration. Histologically, A. calamus differs from the species of Alpinia, in that it has *collenchymatous hypodermis*. Chains of parenchymatous cells in the cortex forming large intercellular spaces, leptocentric vascular bundles, large spherical oil cells and small size of the starch grains. The authors carried out different tests for purity and found that *moisture content*, *total ash*, *extractive values*-ethyl alcohol and water, *total nitrogen* and *sugar content* are higher in the two species of Alpinia than in *Acorus calamus* or 'true Bach'. The authors further observed that the flucrescent behaviour was the maximum in A. calamus. It is felt that the above paramates will help to distinguish the genuine drug from its common adulterants.