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Mini Review

DIAGNOSTIC AGENTS-TYPES AND APPLICATIONS: A DISCUSSION

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INTRODUCTION

Although biochemistry has long been recognized as a fundamental basis for each of the separate biological and medical sciences, it has now become more and more a common link between biological research and all the medical disciplines, such as physiology, pathology, pharmacology, and so on. Therapy has become increasingly directed towards the correction of pathological conditions by purposeful alteration of biochemical processes. Thus, over the years, a number of substances from the group of biochemicals have been used as Diagnostic Agents beside their use in medicine. The past few decades have been marked by an unprecedented development of diagnostic research. Thus, including the simple diagnostic procedures, enzymes studies, cancer research, vitamin research and others have been helped by the introduction of test reagents.

DIAGNOSIS

Mainly diagnosis is divided in two types :

1. The determination of the nature of a case of disease .
2. The art of distinguishing one disease from another.

Further, diagnosis is subdivided into twelve categories depending upon the nature of action taken or work-pattern involve to identify a particular disease. These are :

- ***i.*** ***Biological Diagnosis :*** This is based on tests done on animals.
- ***ii.*** ***Clinical Diagnosis :*** This is based on signs and symptoms of a disease.
- ***iii.*** ***Cytohistologic Diagnosis :*** To detect both benign and malignant by study of exfoliated cells.
- ***iv.*** ***Cytologic Diagnosis :*** By studying the functions of living cells.
- ***v.*** ***Differential Diagnosis :*** By comparing clinical findings in two diseases.
- ***vi.*** ***Direct Diagnosis :*** By exclusion process.
- ***vii.*** ***Laboratory Diagnosis*** **:** By examinations and measurements in laboratory.
- ***viii.*** ***Nivean diagnosis :*** By localization of extent level of a lesion (e.g. tumor).
- ***ix.*** ***Pathologic Diagnosis :*** By observing structural lesions present.
- ***x.*** ***Physical Diagnosis :*** By inspection, palpation, percussion and auscultation.
- ***xi.*** ***Provocative Diagnosis :*** By induction of a condition into a diseased body.
- ***xii.*** ***Serum Diagnosis :*** By analysis of serum.

DIAGNOSTIC AND DIAGNOSTIC AGENTS

Diagnostic is a process of distinguishing symptoms, and the chemicals which are used to distinguish symptoms are known as diagnostic agents.

Basically, diagnostic agents includes chemical compounds of inorganic or organic nature, most of these being modified in their structural moeity, so as to become specific for their test reactions. These modifications make them biochemicals, depending upon their constitution and functional groups. Inorganic chemicals are not directly functioning as diagnostic agents, but their use, by some way, is essential either to control the reaction process or to provide the necessary conditions for the systematic

analysis. Beside the organic reagents used, dyes and stain are an important class of diagnostic agents especially for quantitative determination by colorimetry, which is now the best tool for diagnosis.

Radioactive tracers are extensively used in routine clinical diagnosis. Important examples are, studies of the functioning of thyroid gland and to locate the exact site of the tumors of brain by using radioactive iodine, studies of blood circulation time using radioactive sodium and chromium, studies of obscure anaemias and other blood disorders using radioactive iron and studies of important body functions such as digestion, metabolism and excretion. The functioning of different parts and organ systems of the body such as the liver, the kidneys, etc. is also studied by using radioactive isotopes, thus enabling the diagnosis of different disease states.

Broadly, we can divide the various compounds used as diagnostic agents into four major classes as :

A. Inorganic and organic compounds used directly.
B. Dyes and stains specifically for use in end point or initial rate colorimetry.
C. Radioactive tracers.
D. Culture-media chemical-basic constituent being Agar.

It is worthwhile to discuss some of the compounds which are used either as diagnostic agents or as subsidiary agents to control the conditions and the medium of reactions (pH etc.) and which represent the above classes.

(A) Inorganic and Organic Compounds Used

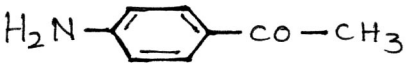
i. Ferric ammonium citrate: it is used as bacteriological ingredient.

ii. Sodium chloride: it is used as tissue culture grade.

iii. Bees wax: It is used for histology.

iv. Digitonin: it is used for cholesterol determination.

v. p-Aminoacetophenone, C_8H_9ON.

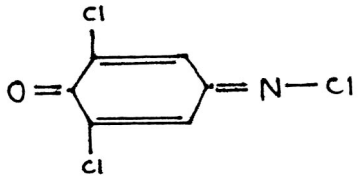


It is a chemical reagent used in a simple method for the chemical determination of urinary thiamine based upon the PrebludaMcCollum reaction[1].

vi. Bilirubin, $C_{33}H_{36}O_6N_4$

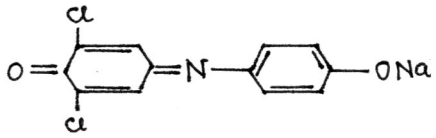
Standard in the calorimetric determination of bilirubin in blood[2], i.e. the estimation of serum bilirubin[3].

vii. Dichloroquinone Chlorimide , $C_6H_2ONCl_3$



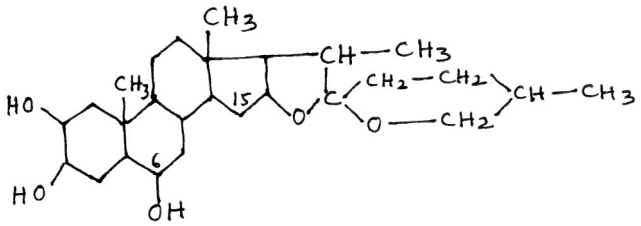
This reagent is used in the diagnostic study of the urinary excretion of vitamin B_6 by a colorimetric method. [4]

viii. Dichlorophenol-indophenol, $C_{12}H_6O_2NCl_2Na$



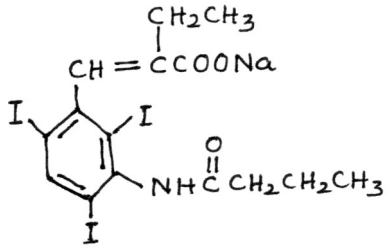
Used in the diagnosis of vitamin C-sub-nutrition by urine analysis, with a note on the antiscorbutic vlaue of human milk[5].

ix. Digitonin, $C_{56}H_{92}O_{29}$



A modified Digitonin used as diagnostic agent for the determination of cholesterol[6].

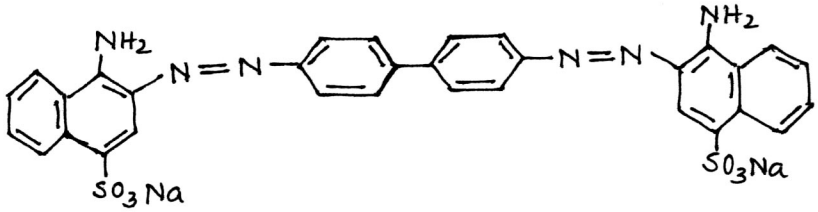
x. Buniodyl, 2-[[2,4,6-Triiodo-3-[(1-oxobutyl)amino]phenyl]methylene] butanoic acid monosodium salt[7], $C_{15}H_{15}I_3NNaO_3$.



It gives crystals from water, slightly soluble in water, used as a diagnostic aid in radiopaque medium.

(B) Dyes and Stains

i. Congo Red: 3,3'-[[Biphenyl]-4,4'-diylbis(azo)-bis [4-amino-1-napthalene sulfonic acid] disodium salt, $C_{32}H_{22}N_6Na_2O_6S_2$



It is a brownish-red powder, soluble in H_2O and ethanol, insoluble in ether. Used as reagent dye, biological stain as diagnostic aid (amyloidosis)[8]

ii. Acid fuchsin: A widely used plasma stain for connective tissue and stain for bacteriology.

iii. Acridine Orange: A biological stain, fluoroscent dye for cytochemical staining.

iv. Basic fuchsin: Used for staining bacilli, especially influenzae and tubercle, in tissues

v. Giemsa Stain: Stain used for blood and malarial parasites.

vi. Methyl Green,: A biological stain used as general tissues stain for differentiation of bacteria.

vii. Methylene Blue: A stain for elastic fibres and connective tissue and for tubercle and leprae bacilli in mammalian tissue.

viii. Neutral Red: A general histological and bacteriological stain.

ix. Orange-G: A collagen stain for connective tissue.

x. Orcein : A histological staining reagent.

(C) Radioactive Tracers[9,10]

Name and Symbol	Form	Use (Diagnostic)
Americium ^{241}Am	Encapsulated source	In bone mineral analyzer.
Chromium ^{51}Cr	Sodium chromate (Labelled red blood cells)	Study of blood volume and red cell survival, spleen imaging; placental localization.
Chromium	Labelled human serum	Placental localization; loss of gastrointestinal

^{51}Cr	albumin	proteins.
Cobalt ^{60}Co and ^{57}Co	Radioactive Vitamin B_{12}	For absence of intrinsic factor (P.A.) or defect in absorption (sprue). Metabolic studies.
Copper ^{64}Cu	Copper versenate Copper acetate	Brain scans for tumors, Study Wilson's disease.
Fluorine ^{18}F	Sodium fluoride (reactor produced)	Bone scan
Gallium ^{67}Ga	Gallium citrate	Tumor seeking agent
Gold ^{198}Au	Colloidal gold	Liver imaging
Indium ^{113m}In	Indium-DTPA	Brain imaging
Indium ^{113m}In	Indium-transferrin	Static cardiovascular blood pool imaging. Hepatic blood pool imaging Placental localization
Indium ^{113m}In	Indium-$Fe(OH)_3$	Perfusion Lung scan
Indium ^{113m}In	Indium-colloid	Static liver imaging; spleen imaging
Indium ^{113m}In	Indium-DTPA	Cisternography
Indium ^{111}In	Indium chloride	Hematopoietic bone marrow imaging; tumour seeking agent
Iodine ^{131}I	Sodium iodide	Thyroid scan. Study action of thyroid and antithyroid drugs; study of chloride space; aid in determining thyroid activity.
Iodine ^{131}I	Diiodofluorescein	Diagnosis and Localization of brain tumors
Iodine ^{131}I	Iodinated serum albumin	Determination of plasma volume, peripheral vascular flow, cardiac output, circulation time and cerebral vascular flow. Diagnosis & localization of brain tumors. Placental localization. Cisternography
Iodine ^{131}I	Macroaggregated iodinated serum albumin	Perfusion lung scan
Iodine ^{131}I	Colloidal microaggregated iodinated serum albumin	Hepatic blood pool imaging
Iodine ^{131}I	Iodinated fibrinogen	Determination of fibrinolytic enzymes *in vitro*
Iodine ^{131}I	Iodinated rose bengal	Liver function *in vivo*-hepatic excretion studies
Iodine ^{131}I	Iodopyracet, Na Iodo hippurate, Na diatrizoate, diatrizoate methyl glucamine, Na diprotrizoate, Na acetrizoate or Na iothalamate	Bilateral renal function test *in vivo* Kidney imaging
Iodine ^{131}I	Iodinated fats or fatty acids e.g. Iodine ^{131}I-triolein	Pancreatic function, intestinal fat absorption
Iodine ^{131}I	Copolymer of p-toluidine vinylpyrrolidone ^{131}I (Tolpovidone Abbott)	Diagnosis of exudative enteropathy
Iodine ^{125}I	Sodium Iodide	Thyroid imaging
Iodine	Iodinated serum albumin	Determination of plasam vol.

^{125}I		
Iodine ^{125}I	Iodinated rose bengal	Liver function-hepatic excretion studies
Iodine ^{125}I	Iodinated fats	Intestinal fat absorption
Iodine ^{125}I	Sealed source	For use in bone mineral analyzer
Iron ^{59}Fe ^{55}Fe	Ferrous citrate $FeSO_4$	Determination of blood vol. with RBC's labelled *in vivo*, study of iron metabolism; blood transfusion studies.
Krypton ^{85}Kr	Gas	Cardiac abnormalities; skeletal muscle, coronary or cerebral blood flow
Mercury ^{197}Hg ^{203}Hg	Chlormerodin	Brain scans for tumors, renal studies for defects, clearance etc.
Phsophorus ^{32}P	Disodium hydrogen phosphate	Determination of blood vol. with RBC's labeled *in vitro*; study of peripheral vascular disease; localization of brain tumors; study of carcinomas of breast
Potassium ^{42}K	Potassium carbonate	Localization of brain tumors; determination of intracellular fluid space
Selenium ^{75}Se	Seleno-methionine	Pancreas imaging
Sodium ^{24}Na	Sodium chloride	Study of peripheral vascular disease, extracellular space, circulation time, formation of cerebrospinal fluid, sodium metabolism.
Strontium ^{85}Sr ^{87m}SR	Strontium nitrate or chloride	Bone imaging in patients with known or suspected malignancies
Technetium $^{99m}Tc.$	Pertechnetate $NaTcO_4$	Brain scan, Blood pool, placental localization, thyroid scan
Technetium $^{99m}Tc.$	Colloidal sulfate	Liver, spleen and bone marrow scans
Technetium $^{99m}Tc.$	Tc albuminate	Heart scan; placental localization
Technetium $^{99m}Tc.$	Tc albuminate macro or microaggregates	Perfusion lung scan
Technetium $^{99m}Tc.$	Tc DTPA (iron ascorbate)	Kidney scan
Technetium $^{99m}Tc.$	Tc DTPA (Tin)	Kidney and brain scans
Technetium $^{99m}Tc.$	Tc stannous polyphosphate, Tc stannous etidronate	Bone scan
Xenon ^{133}Xe	Gas or gas in saline solution	Pulmonary function-ventilation studies, Cerebral blood flow; coronary abnormalities; skeletal muscle blood flow.
Ytterbium $^{169}y_b$	Y_b-DTPA	Cisternography; Brain scan

(D) Culture-media chemical-basic constituent being AGAR

Agar is a gelatin like material obtained from certain seaweeds; it is chemically related to the carbohydrates. A solution in hot water sets to a firm jelly, which is used as a base for **culture media** for growing bacteria.

(i) AC Agar : Used for sterility testing.

(ii) Acetamide Agar : Used for differentiation of nonfermentative gram -ve bacteria, particularly Pseudomonas aeruginosa.

(iii) **Aeromonas isolation medium base** : Used for selective differential isolation of aeromonous hydrophila from clinical specimens.

(iv) **Anaerobic Agar** : Used for isolation and identification of anaerobic pathogens.

(v) **Azide Blood Agar Base** : Used for selective isolation and cultivation of gram +ve coccistaphylococcus and streptococcus species from clinical and non clinical mixed flora.

CONCLUSION

Diagnostic agents are, thus, special chemical compounds which are specific in their reactions by which definite conclusions may be drawn, both qualitative and quantitative regarding the cause of and disease itself. These compounds are helping aids for clinical pathology in general and other branches of medical science. Newer radioactive isotopes, dyes and compounds are proving to be modern diagnostic agents. The more the disease, more the diagnostic agents are to be required.

REFERENCES

1. B.Alexander and J.E.Levi, *J. Biol. Chem*., **146** ,399(1942)
2. A.A.M.Van den Bergh and W.Grotepass, *Lancet*, **I,**1157 (1934)
3. J.Patterson, J.Swale and C.Maggs, *Biochem*., *J*., **52**,100 (1952)
4. J.V.Scudi, K.Unna and W.Antopol, *J. Biol Chem*., **135,**371 (1940)
5. L.J.Harris and S.N.Ray, *Lancet*, **71,**228 (1935)
6. E.J.Pentz and E.M.McArthur, *J. Lab. Clin. Med*., **37,**151 (1951)
7. Cassebaum, Dierbach, *Pharmazie*, **16,**389 (1961)
8. Richardson, Dillon; *Am. J. Med. Sci.*, **73,**198 (1939)
9. Charles Behrns, E. Richard King, James W.J. Corpenter, *Atomic Medicine* (The Williams & Wilkins Co., Baltimore, **5th ed**. (1969).
10. Yen Wang, Editor, CRC Hand book of Radioactive Nuclides, (The Chemical Rubber Co., Cleveland, Ohio (1969).

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