



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

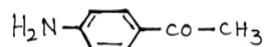
Diagnostic is a process of distinguishing symptoms, and the chemicals which are used to distinguish symptoms are known as diagnostic agents.

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.

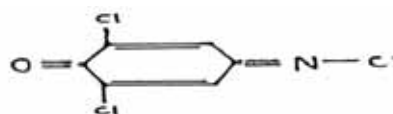
(A) Inorganic and Organic Compounds Used

- 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 .



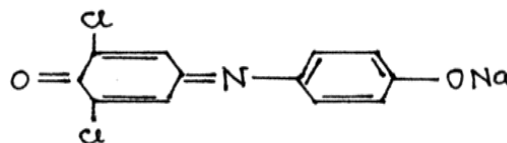
It is a chemical reagent used in a simple method for the chemical determination of urinary thiamine based upon the PrebludaMcColum reaction .

- vi. **Bilirubin**, $C_{33}H_{36}O_6N_4$ Standard in the calorimetric determination of bilirubin in blood, i.e. the estimation of serum bilirubin
- vii.



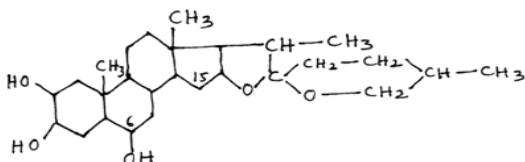
This reagent is used in the diagnostic study of the urinary excretion of vitamin B6 by a colorimetric method.

- viii.



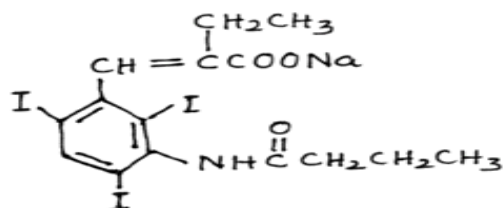
Used in the diagnosis of vitamin C-sub-nutrition by urine analysis, with a note on the antiscorbutic vlaue of human milk.

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



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

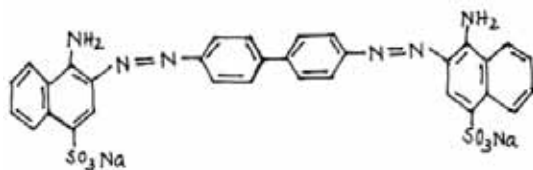
x. Buniodyl, 2-[[2,4,6-Triiodo-3-[(1-oxobutyl)amino]phenyl]methylene]butanoic acid monosodium salt, $C_{15}H_{15}I_3NNaO_3$



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-naphthalene sulfonic acid]



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)

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

- iii. Acridine Orange:** A biological stain, fluorescent 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) (Refer Table 1)

(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.

Table 1: (C) Radioactive Tracers

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 ^{51}Cr	Labelled human serum albumin	Placental localization; loss of gastrointestinal 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 ^{113}mIn	Indium-DTPA	Brain imaging
Indium ^{113}mIn	Indium-transferrin	Static cardiovascular blood pool imaging. Hepatic blood pool imaging Placental localization
Indium ^{113}mIn	Indium-Fe(OH) ₃	Perfusion Lung scan
Indium ^{113}mIn	Indium-colloid	Static liver imaging; spleen imaging
Indium ^{111}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	Hepatic blood pool imaging

Table 1 Continues....

¹³¹ I	Iodinated serum albumin	Iodine	Iodinated fibrinogen Determination of fibrinolytic enzymes <i>in vitro</i>
¹³¹ I Iodine	Iodinated rose bengal		Liver function <i>in vivo</i> -hepatic excretion studies
¹³¹ I Iodine ¹³¹ I	Iodopyracet, Na Iodo hippurate, Na diatrizoate, diatrizoate methyl glucamine, Na diprotrizoate, Na acetrizoate or Na iothalamate		Bilateral renal function test <i>in vivo</i> Kidney imaging
Iodine	Iodinated fats or fatty acids e.g. Iodine ¹³¹ I-triolein		Pancreatic function, intestinal fat absorption
¹³¹ I Iodine	Copolymer of p-toluidine vinylpyrrolidone ¹³¹ I (Tolpovidone Abbott)		Diagnosis of exudative enteropathy
¹³¹ I Iodine	Sodium Iodide		Thyroid imaging
¹²⁵ I Iodine	Iodinated serum albumin		Determination of plasam vol.
¹²⁵ I Iodine	Iodinated rose bengal		Liver function-hepatic excretion studies
¹²⁵ I Iodine	Iodinated fats		Intestinal fat absorption
¹²⁵ I Iodine	Sealed source		For use in bone mineral analyzer
¹²⁵ I Iron	Ferrous citrate FeSO ₄		Determination of blood vol. with RBC's labelled <i>in vivo</i> , study of iron metabolism; blood transfusion studies.
⁵⁹ Fe ⁵⁵ Fe			
Krypton	Gas		Cardiac abnormalities; skeletal muscle, coronary or cerebral blood flow
⁸⁵ Kr			
Mercury ¹⁹⁷ Hg ²⁰³ Hg	Chlormerodin		Brain scans for tumors, renal studies for defects, clearance etc.
Phosphorus	Disodium hydrogen phosphate		Determination of blood vol. with RBC's labeled <i>in vitro</i> ; study of peripheral vascular disease; localization of brain tumors; study of carcinomas of breast
³² P			
Potassium	Potassium carbonate		Localization of brain tumors; determination of intracellular fluid space
⁴² K			
Selenium	Seleno-methionine		Pancreas imaging
⁷⁵ Se			
Sodium	Sodium chloride		Study of peripheral vascular disease, extracellular space, circulation time, formation of cerebrospinal fluid, sodium metabolism.
²⁴ Na			
Strontium	Strontium nitrate or chloride		Bone imaging in patients with known or suspected malignancies
⁸⁵ Sr ⁸⁷ mSR			
Technetium	Pertechnetate NaTcO ₄		Brain scan, Blood pool, placental localization,

Table 1 Continues....

⁹⁹ mTc. Technetium	Colloidal sulfate	thyroid scan Liver, spleen and bone marrow scans
⁹⁹ mTc. Technetium	Tc albuminate	Heart scan; placental localization
⁹⁹ mTc. Technetium	Tc albuminate macro or microaggregates	Perfusion lung scan
⁹⁹ mTc. Technetium	Tc DTPA (iron ascorbate)	Kidney scan
⁹⁹ mTc. Technetium	Tc DTPA (Tin)	Kidney and brain scans
⁹⁹ mTc. Technetium	Tc stannous polyphosphate, Tc stannous etidronate	Bone scan
⁹⁹ mTc. Xenon	Gas or gas in saline solution	Pulmonary function-ventilation studies, Cerebral blood flow; coronary abnormalities; skeletal muscle blood flow.
¹³³ Xe		
Ytterbium	Yb-DTPA	Cisternography; Brain scan
¹⁶⁹ yb		

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.

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