EXPERIMENTAL ALTMETRICS AS A PRECURSOR TO ARTIFICIAL INTELLIGENCE. OPTIMAL PROCESSING AND PHARMACEUTICAL FORMULATION INVOLVING A SELECTIVE EXPERIMENTAL DIAGNOSTIC AND TREATMENT PROTOCOL

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Abstract. The effects of the surfactant adsorption on the surface of a free liquid drop, immersed in an unbounded liquid (the densities of the two bulk liquids are equal) are studied. The interfacial tension gradients, caused by the surfactant applied on the drop surface, generate surface forces within the boundary region of the free drop, leading to a surface flow (known as Marangoni flow). As a result of this flow, which causes the motion of neighboring liquids by viscous traction, a hydrodynamic pressure force (named Marangoni force) is generated which acts on the free drop surface. The aim of this research study is to correlate the effects of interfacial tension gradients, in a real surface flow, with the forces of hydrodynamic pressure, acting on the free drop surface. The Marangoni force is examined on nondeformable and deformable free drops. Dynamics of free liquid drops is known as the interfacial Marangoni effect. This effect has an important impact on surface flow of liquids in the absence of gravity, as well as in advanced fundamental research in physical chemistry, colloidal science, biological phenomena and in medical applications.

Keywords: medical analysis; imaging; functional exploitations; integrated AI; compatibility; biometry

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1. Introduction

Experimental altmetrics is the summative model for determining the state of health and monitoring the evolution of a patient's health during the treatment period,

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involving modern methods of medical analysis in a system of digitisation and digital assay and cross-checking between interdisciplinary techniques. It includes both the field of medical analysis, which includes biochemical, hematologic, immunologic, serologic, bacteriologic, virologic, mycologic, parasitological, histologic, cytologic, pathologic, and other types of analysis by examining samples from the human body (blood samples, urine, CSF, secretions, tissues, etc.) and the field of imaging and functional explorations [1-3].

The interpretation of analytical and imaging data allows the validation of real evidentiary characteristics related to health status and the establishment of optimal values for falling within the range of its parameters or characteristics.

After 1990, following the model of some international organisations for the attestation and accreditation of medical analysis, imaging, and functional testing laboratories, several unique national accreditation bodies for laboratories were developed in our country (RENAR – Romanian Accreditation Association, National Accreditation Centre – MOLDAC in the Republic of Moldova and Romanian Standardisation Association – ASRO), which allow the accreditation of analytical methods, the evaluation of their operational conformity, together with the verification, validation and approval of the supporting apparatus, which are certified by the Romanian Bureau of Legal Metrology (for quantitative measurement techniques) and the National Agency for the Regulation of Nuclear and Radiological Activities of the National Commission for the Control of Nuclear Activities – CNCAN (for techniques operating with radioactive sources). They provide technical expertise and specialised interface in Romania's relations with international bodies and organisations [4-7].

Moreover, when acquiring instrumental techniques for analysis, imaging, and functional exploitations, the suppliers are also subject, before commercialisation, to quality attestation/accreditation evaluation (fulfilment of application requirements).

Even in these conditions, several values and units of measurement of data in very many medical analysis bulletins have different ranges within the optimal limits, which is why they are not recognised when transferring the patient to other hospitals abroad.

For these reasons, efforts are being made to reach a consensus and develop standards that will be recognised and accepted in health assessment surveys. Particular attention has also been paid to pattern recognition, problem-solving, and decision-making [8]. The interest in the last decade in involving altmetrics in medicine has led to the development of software such as TensorFlow, Keras, and PyTorch, as well as commercial software such as PLS_Toolbox and Solo 9.0 [9].

Based on experiences already in nutritional practice, recommendations for diets specific to each individual and their biorhythm are made by correlating blood groups with the nature and value of foods. Over the last ten years, many have claimed that the so-called 'blood group diet' is very effective. This diet involves eating certain foods according to the blood group to lower the risk of certain diseases and maintain good health. However, a 2013 scientific study concluded that there was no clear evidence of a direct link between diet and blood type.

By correlating the biorhythm, linked to the date of birth, time, and place, with a series of biometric/anthropometric characteristics (weight, height, age, etc.), it is possible to estimate the gradual development of an individual's potential/livelihood about exogenous (chemical pollution, microbiological and radiological contamination, including exposure to electromagnetic radiation in the UV, vis and IR range, health standards and nutritional value of food, etc.) and endogenous (health and disease history of first-degree relatives, intensity/rate and frequency of cases, genotype, etc.) factors.

Another essential trait with altmetric implications, frequently addressed by Artificial Intelligence (AI) through collateral algorithms, is blood type, which is genetically inherited from parents, like other traits. Children inherit half of the genetic dowry of both parents. The phenotype of children depends on the genes expressed in their genotype and intrinsic and extrinsic epigenetic factors.

In the prevention and treatment of a condition (disease), one needs to know the onset (through chemical intoxication, microbiological contamination, etc.), then the clinical changes, followed by cure/convalescence, chronicization or malignancy, all of which are correlated with the determining assessing factors (exogenous and endogenous). Medical altmetrics will also consider the patient's family history or the anamnesis of the health status of first-degree relatives, as well as the patient's biorhythm.

Currently, medical analysis laboratories and those for imaging or functional explorations are endowed with modern equipment and high-quality reagents, and well-trained specialists are involved in their use. Most of the equipment is digitised, accompanied by software for processing material samples taken from patients and automatically interpreting the results by highlighting those within normal limits.

The paper presents the current aspects of medical altmetrics involved in assessing a patient's health status using modern analysis methods in the digitisation assay system and corroboration between interdisciplinary techniques. It includes biochemical, haematological, immunological, serological, bacteriological, virological, mycological, parasitological, histological, cytological, pathological, and other types of analysis by examining samples from the human body (blood group, urine, CSF, secretions, tissues, etc.), as well as imaging or functional explorations.

They are standardised by accreditation-attestation systems of quality and conformity of characteristics, which are unanimously accepted worldwide. Particular attention is paid to determining blood group by the AB0/ Jan Jansky system and the Rhesus factor (Rh), which has both a medical and personal importance, being linked to the risk of developing certain diseases (coronary pathologies, gastric cancer, peptic ulcer, memory, thinking and reasoning problems associated with dementia, etc.) and which provides essential information to specifically guide lifestyle to reduce the risk of developing certain associated health conditions. In addition, in diagnosis and treatment, family history or health history of first-degree relatives and the patient's biorhythm will be considered.

2. Methodology and protocols

2.1. Accreditation of medical laboratories

Medical testing laboratories are grouped according to SR EN ISO 15189:2023 accreditation requirements (Code: DR-LM-03) and take into account EA, ILAC, and MOLDAC (for the Republic of Moldova) documents applicable to this standard to ensure a uniform and consistent application.

Within this approach, a series of reference documents are used for Romania, unanimously accepted in Europe [10], too, among which we mention:

- ➤ Law No. 235 of 01.12.2011, on accreditation and conformity assessment activities with subsequent amendments.
- Quality and competence requirements for medical laboratories. SM SR SR EN ISO 15189:2014.
- ➤ Requirements for safety, for medical laboratories. SM SR ISO 15190:2012 and SM SR ISO ISO/TR 22869:2012.
- ➤ Guide for the implementation of ISO 15189:2003 in medical laboratories. ISO/TS 22367 on error reduction through risk management and continuous improvement.
- ➤ Standard on in vitro diagnostic medical devices SM EN ISO 17511:2014 Measurement of quantities in samples of biological origin.
- ➤ Metrological traceability of values assigned to calibrators and control materials. SM SR EN ISO ISO 18153:2010 for in vitro diagnostic medical devices.
- ➤ Measurement of quantity in biological samples. Metrological traceability of values for the catalytic concentration of enzymes assigned to calibrators and control materials. SM SR EN ISO/IEC 17000 2006
- Conformity assessment and general principles SM SR EN ISO/IEC 17011:2006.
- ➤ General requirements for accreditation bodies requiring conformity assessment SM SR EN ISO/IEC 17000:2006.

➤ National Accreditation Body rules and procedures. EA application documents: EA – 4/14:2003 informative Selection and Use of Reference Materials; EA – 4/16:2003 guidance EA Guidelines on the Expression of Uncertainty in Quantitative Testing.

In addition to the documents above, those for the Republic of Moldova – MOLDAC [* * *, www.acreditare.md] are used as follows:

- ➤ Policy P-02 on the use of proficiency testing and other interlaboratory comparisons in the accreditation process;
- ➤ Policy P-03 on traceability of measurements;
- ➤ Policy P-04 on dealing with non-conformities;
- ➤ Policy P-07 on handling National Accreditation Body (CAB) objections concerning the names of assessment team members;
- ➤ Policy P-08 on rules for using accreditation symbols and references to accreditation: RA and CA (rules for accreditation and general criteria for accreditation).

When accrediting laboratories under the jurisdiction of other states, the legal liability requirement must be ensured and assessed by a legal person competent in that state's law who can adequately support the fulfilment of this requirement. The laboratory must have valid public liability insurance unless the laboratory is insured by the state by operation of law, and the insurance must be both contractual and public liability.

The laboratory must have a rigorously documented procedure for preparing the analytical report, for each Analytical Bulletin, so that the results are presented accurately, clearly and unambiguously and establish the format and medium of the report (paper or electronic system) and how it is communicated.

According to the standards of European countries, also accepted by Romania, the analysis bulletins must bear the stamp of an authentic document, together with a series of essential valuable attributes, such as high specificity in correlation with the medical case, including absolutely all the data related to the laboratory, analysis, instrumental technique, measurement units, limits of the normal range of variation of the determined data, coherence and clarity, etc.

The report must contain sufficient information for interpretation, and in the case of a delayed result, there must be a process for notifying the applicant. It should also include comments on the quality of the sample (whether the sample is compliant/non-compliant with the acceptance criteria) and critical results.

The content of the *Analytical Report* will include the following: clear identification of the issuing laboratory, clear identification of the examination including method, identification of examinations performed by the laboratory/subcontractor, identification of the patient, on each page, name and contact details of the applicant

(physician, insurance company), date of primary sample collection and time, type of primary sample measurement/determination procedure (where applicable), examination results reported in SI units, units traceable to SI units or other applicable units, biological reference ranges, clinical decision values and/or charts/nomograms supporting clinical decision values (if applicable), interpretation of results – if applicable (Note: Full interpretation of results requires the context of clinical information, which may not be available at the laboratory and other comments such as: cautionary or explanatory notes – for example: results/interpretations from contracted laboratories, identification of examinations performed as part of a research or development program and for which no specific measurement performance requirements are available, identification of the person reviewing the results obtained, presentation of results and persons authorising the release of the report, date and time of release, page number of total number of pages).

The laboratory must document the case of positive results for notifiable communicable diseases and how the early warning legislation is implemented. Laboratories must follow RENAR and MOLDAC policies on using accreditation symbols and references to accreditation when preparing the Analytical Bulletin.

The lab must have well-documented procedures for releasing results, by whom, and to whom they are released. Then, make sure that the report states the status of the primary sample, if there are any alert values on the report, and when to notify the physician immediately, with records of the time and person notified. The result of the examination, the person who submitted and any difficulties encountered in submitting, make sure the results are legible, free of mistakes, and if a partial report is issued, always issue a final report as well, and ensure a process for the telephonic transmission of results (with the certainty that the results reach only authorised recipients), that there is a record of the results transmitted orally and that these are followed by the issue of a written report. (Note: For the results of specific examinations – for example, examinations for certain genetic or infectious diseases, special advice may be required. In this case, the laboratory should endeavour to see which results with serious implications should not be communicated directly to the patient without the possibility of appropriate counselling).

Results from which patient identifiers have been removed may be used for statistical purposes in epidemiology, demography, or other statistical analyses.

Automated selection and reporting of results shall be based on a procedure in which the criteria for automated selection and reporting are defined, approved, readily accessible, and understandable to staff, who decide to change nonsense, unlikely, or critical values, whether there is a process that shows the presence of interferents (haemolysis, lipemia, etc.), the results selected for automated reporting must be identifiable at the time of review, and whether the process for early suspension of automated selection and reporting is established.

A revised report must be identified as a revision and include reference to the date and patient identity in the original report; the user is made aware of the revision, and the revised record shows the time and date of the change and the name of the person responsible for the change. Mentions of the original report remain in the record when revisions are made. The results made available for clinical decision-making and the revision of that clinical decision must be retained in subsequent cumulative reports and identified as revised.

2.2. Role and functions of the laboratory accreditation certificate

As is well known, attestation is the issuing of a statement, based on a decision following an assessment analysis, that the applicable requirements have been met and demonstrated in practice. So, accreditation is a third-party attestation, which is the official confirmation that a body is competent to carry out this work. It contributes to increasing the competitiveness of products and services in the context of globalising markets.

Accreditation confers confidence in the technical competence, impartiality and integrity of the bodies and laboratories that apply for/perform conformity assessment, then contributes to promoting the principle of free movement of products and services, promotes the protection of the life, health and safety of individuals, the environment and the interests of patients and the health care system.

Accreditation aims to fulfil the basic principles outlined above.

Accreditation offers several advantages, such as:

- ➤ Minimisation of risks;
- > Avoidance of multiple assessments;
- ➤ Increasing the confidence of patients and healthcare staff;
- ➤ Reducing the costs of recognising experimental data/results in the international system;
- > Reduce overheads.

Accreditation is essential for the functioning of a quality-oriented market vis-à-vis the public authorities and the conformity assessment bodies.

For accreditation, the *infrastructure*, i.e., *the system of conditions* (buildings, workspaces, and associated utilities), *equipment* and *support services* required for the operation of the laboratory, specialised staff and job description, security and protection systems (preventive elements), work program (if applicable, detailed by laboratories and services) must be declared and detailed.

The laboratory presentation report will focus on each distinguishing characteristic or feature, grouped into different classes, such as: physical (electrical, optical, magnetic, radioactive, etc.), chemical, biological, sensory (relating to smell, taste, sight, hearing, touch), functional (speed, acceleration).

The activity of laboratory accreditation comprises:

- initiating the attestation, which consists of analysing the application and the submitted documents;
- analysing the documents;
- > pre-assessment of the testing/analytical laboratory (at the client's request);
- on-site evaluation of the activity of the analytical/testing laboratory (evaluation of the set of documents, access to the laboratory's premises to verify its technical competence according to the declared scope of attestation, elimination of non-conformities found during the laboratory's evaluation or rectification of non-conformities, planning of surveillance visits, and participation in any proficiency tests (PT) or inter-laboratory tests/laboratory tests (ILC) that the accreditation institute deems necessary;
- > the decision on accreditation;
- > issuing the attestation certificate.

2.3. Medical analysis and instrumental techniques

Nowadays, medical analysis laboratories and laboratories for imaging and functional explorations are equipped with modern equipment and high-quality reagents, and well-trained specialists are trained to use them. Most machines are digitised, accompanied by software for processing material samples taken from patients and automatic interpretation of the results, highlighting the fall within normal limits.

The reference ranges and the unit of measurement (MU) are known for each sample type for medical analysis. For example, Tables 1-5 show the assays for serum, plasma, and blood samples analysed by the Biochemistry laboratories, which, compared to the reference range, will fall within the assay results.

Table 1. Analys	sis for serum sampl	les – Biochemistr	y/Atellica Solution ((in alphabetical order)

Analysis	Method/Technique	Reference range	UM
Uric acid	Spectrophotometry	3.7 - 9.2	mg/dL
ALT	Spectrophotometry	10 - 49	U/L
Amylase*	Amylase	30 – 118	U/L
AST	Spectrophotometry	0 - 34	U/L
Direct bilirubin	Spectrophotometry	0.0 - 0.3	mg/dL
Total bilirubin	Spectrophotometry	0.3 - 1.2	mg/dL
Indirect bilirubin*	-	0.0 - 0.70	mg/dL

Direct bilirubin	Spectrophotometry	0.0 - 0.3	mg/dL
Cholesterol	Spectrophotometry	0 - 200	mg/dL
Cholesterol – HDL	-	40 - 60	mg/dL
Cholesterol – LDL	-	130.000 - 150.000	mg/dL
Creatinine	Spectrophotometry	0.70 - 1.30	mg/dL
Fer	Spectrophotometry	65-175	μg/dL
Alkaline phosphatase	Spectrophotometry	46 – 116	UL
GGT	Spectrophotometry	0 -73	UL
Glycemia	Spectrophotometry	74-106	mg/dL
Glycosylated haemoglobin	-	4 - 6	
LDI/LDH*	Spectrophotometry	120 – 246	UL
Total protein	Spectrophotometry	5.7 - 8.2	g/L
Triglyceride	Spectrophotometry	0 - 150	mg/dL
Urea	Spectrophotometry	9 – 39	mg/dL

^{*} These analyses and interpretations are not covered by RENAR accreditation

Table 2. Analysis for serum samples – Serology/Atellica Solution Turbidimetry (in alphabetical order)

Analysis Method/Technique		Reference range	UM
PCR	Turbidimetry	0.0 - 0.5	mg/dL

Table 3. Analysis for plasma samples – PT/INR (in classical order)

Analysis	Method/Technique	Reference range	UM
PT s/ without oral anticoagulant therapy	Coagulation/ SYSMEX CS 2500	10.40 – 14.30	sec
PT s/ with oral anticoagulant therapy	Coagulation/ SYSMEX CS 2500	23 – 40	sec
AP/ without oral anticoagulant therapy	Coagulation/ SYSMEX CS 2500	70 – 120	%
AP/ with oral anticoagulant therapy	Coagulation/ SYSMEX CS 2500	15 -40	%
INR/ without oral anticoagulant therapy	PT/INR*	0.85 – 1.25	
INR/ with oral anticoagulant therapy	PT/INR*	2.0 – 3.5	
APTT	APTT*	22.10 - 28.10	sec
Fibrinogen	Fibrinogen*	1.80 - 3.50	g/L

^{*} These analyses and interpretations are not covered by RENAR accreditation

Table 4. Tests for blood samples – Complete blood count* (in classical order)

Analysis	Method/Technique	Reference range	UM
PCT	Haematology	0.12 - 0.36	%
WBC	Haematology	4 – 10	10 ³ /ul
NEU	Haematology	4 - 7.5	10 ³ /ul

NEU%	Haematology	40 - 75	%
PDW	Haematology	25 – 65	%
LYM	Haematology	1.5 - 6.5	10 ³ /ul
LYM%	Haematology	20 – 45	%
MONO	Haematology	0.3 - 1.0	10 ³ /ul
MONO%	Haematology	2.0 - 8.0	%
EOS	Haematology	0.1 - 0.85	10 ³ /ul
EOS%	Haematology	0.0 - 0.5	%
BASO	Haematology	0.0 - 0.2	10 ³ /ul
BASO%	Haematology	0.0 - 0.2	%
RBC	Haematology	4.1 - 5.7	10 ³ /ul
HGB	Haematology	13.0 – 18.0	g/dL
HCT	Haematology	37 – 54	%
MCV	Haematology	80 - 95	FE
MCH	Haematology	26 -34	pg
MCHC	Haematology	32 - 36	g/dL
ROV	Haematology	11.5 – 14.5	%
PLT	Haematology	150 – 450	10 ³ /ul
MPV	Haematology	7.2 - 11.1	FE
Glycosylated	HbA1c level	5.7 - 6.5	%
haemoglobin/glycated			
haemoglobin percentage			

^{*} These analyses and interpretations are not covered by RENAR accreditation

Table 5. Analysis for serum samples – Immunology/Atellica Solution Immunology (in classical order)

Analysis	Method / Technique	Reference range	UM
CA 19-9*	Chemiluminescence	0.00 - 37.00	U/mL
CEA*/Non-smokers	Chemiluminescence	₹ 5.0	ng/mL
CEA*/Smokers	Chemiluminescence	< 10.0	ng/mL
TPSA	Chemiluminescence	0.21 - 6.67	ng/mL

^{*} These analyses and interpretations are not covered by RENAR accreditation

Urine examination or analysis (urinalysis and uroculture) is a diagnostic test that helps to identify substances and cellular material in the urine associated with various metabolic and kidney disorders. The analysis provides indications about the presence of urinary tract infections, bleeding, urinary stones or certain blood diseases such as diabetes or hepatitis.

The analysis of the physical and chemical characteristics of urine is performed in the laboratory and usually involves three steps: visual examination (the colour, clarity, cloudiness and concentration of the urine is assessed), dipstick test (the chemical composition of the urine is examined using a test strip) and microscopic examination (to identify bacteria, cells and cell parts). The urine is tested for: colour, **acidity (pH), concentration in** components (traces of blood, protein, lipids, sugar, ketones, bilirubin, etc.) and specific gravity, indicating urinary tract or kidney disorders and evidence of infection where particles are concentrated in the urine. Along with the urine test, additional tests are often necessary if any of the following characteristics record above-average levels: white blood cells (leukocytes) – a sign of infection. Red blood cells (erythrocytes) – may signal kidney disease, blood disease, or bladder cancer, epithelial cells – a sign of a tumour, but most often, indicate that the urine sample was contaminated during the test and that a new sample is needed, bacteria or enzymes – may indicate an infection, tube-like proteins – may form as a result of kidney disorders, crystallites – a sign of kidney stones.

Usually, a urine examination is not enough to establish a diagnosis. Depending on why the doctor recommended the test, abnormal results may or may not require further tests. The doctor analyses the results, in conjunction with the results of other tests or additional tests, to determine the next steps in treatment.

Concerning imaging techniques or functional explorations, these include: electrocardiography (ECG/EKG), computer tomography (CT) or computed tomography (by areas: cerebral, thoracic, abdominal, angio-coronary, etc.), X-ray or gamma radiography for the thoracic, abdominal, bone, pulmonary, urinary, etc. system, abdominal, breast, cardiac, transfontanellar, transoesophageal, hip, etc., ultrasound, involving complex apparatus or instruments operated by specialists with specific training. Among the functional explorations, Table 6 shows a model of an analysis report.

Table 6. Functional explorations – ultrasound scanner

Analysis	Method/Technique	Results
Ultrasound	Abdominal ultrasonography	Description liver – homogeneous/heterogeneous structure (CBIH, VP, CBP), cholecyst – sediment, pancreas, kidney, spleen (VU), prostate

Blood glucose level

Normal blood glucose levels range from 70 to 130 mg/dL (3.9 - 7.2 mmol/L) before a meal and below 180 mg/dL (10 mmol/L) 2 hours after a meal. These values may vary depending on age, health status, diet, and treatment.

The European standard for fasting blood glucose is >/=126 mg/dL, and the American Diabetes Association recommends a normal value below 154 mg/dL.

Based on our research on compositional formulations of active principles from medicinal plants, fruits and vegetables used in improving and keeping blood glucose values for type 2 diabetes mellitus (T2DM) within the closest possible limits, formulas for the dosage of the amount of tea used were developed for the following ranges: normal 90-130 mg/dL, reversible in a short time, of the order of minutes; between 130 and 150 mg/dL, reversible in an average time of up to 4. ...6 hours; between 150 and 200 mg/dL, reversible in a long time up to 10....12 hours; between 200 and 250 mg/dL, hardly reversible, more than 24 hours; between 250 and 300 mg/dL (the limit where it is often necessary to inject on the recommendation of the attending physician insulin from the NovoMixt (30% soluble insulin aspart — 70% crystallised insulin aspart with protamine), NovoRapid (100% insulin aspart) and Toujeo slow (16.37 mg insulin glargin) cles.

For the first three reversible groups, blood glucose can be improved by exercise (walking for at least 30 min) and diet, assisted by anti-glycaemic teas based on synergistic herbal compositions.

Most diabetologists recommend oral hypoglycaemic or antidiabetic drugs from the biguanide group (metformin, phenformin, and metformin), thiazolidinedione (glitazone), sulfonylurea derivatives (sulfonylurea and antidiabetic sulphonamides), alpha-glucosidase inhibitors (acarbose), glinides and glycosides (SGLT-2 inhibitors).

It should be pointed out that some patients have been known to develop acidosis following treatment with such synthetic oral antidiabetic drugs, with effects that are difficult to tolerate.

There are also many common medical recommendations for diabetes control. Consumption of oral hypoglycaemic drugs gives prominent side effects, and so far, no permanent effective remedy is available for the complete recovery of diabetes mellitus.

Until effective medication procedures are established to reduce the incidence of the disease, complementary (in the form of dietary supplements containing plants and herbs) and alternative medicines should be used as complementary medicines. WHO has prioritised herbal and herbal food supplements as core medicines to improve diabetes because they have no side effects, are accessible, and are low-cost. Their administration can give them medicinal quality if extracted in pure form. Some herbal anti-diabetic formulations, such as those made in Romania (Diafitosan, Diaform, Dialine, Diastine, Diaprin, etc.) or other countries (Arth, Diabecon, Diabecure, Dia-care, Churna, Syndrex, Quath, Vati, etc.) are available on the market. The problem with these preparations is related to identifying the bioactive compounds in each herbal component, the minimum effective doses, and the effect on metabolic pathways, which need to be rigorously checked by physicians to increase their acceptability. These observations allow researchers to develop not

only herbal foods but also medicines that are nutritious, economical, and with improved functionality.

Blood group, its role, and altmetric implications

An essential feature in medical altmetrics is the knowledge of the blood group (through the AB0 system or/and the four Roman numerals established by Jan Jansky) and the Rh factor or system. Recent studies [www.actualno.com] seem to confirm the theory formulated in the 1930s by the Japanese professor *Takeji Furukawa*, who argued that blood groups can influence a person's *traits*, with direct implications for daily life, work, and spirit. In Japan, even when interviewing for a job, job applicants are asked about their blood group so that the employer can understand the candidate's personality.

Human blood groups are due to antigens on red blood cells (red blood cells, erythrocytes). More than 400 antigens have been identified on erythrocytes, which are grouped into erythrocyte systems such as MNSs, Lutheran, Kell, Lewis, Duffy, Kidd, Xy, etc., which are, however, less critical in current medical practice. Regarding clinical implications, the two basic systems – AB0 and Rh – remain, as neglecting them can lead to incompatibility in blood transfusions and pregnancy.

The AB0 system was discovered in 1901 by the Austrian *Karl Landsteiner*; the AB0 system is based on two agglutinogen proteins (A and B antigens) present on the erythrocyte membrane and two agglutinins (A or α and B or β) present in the blood serum. Based on these factors, people fall into four blood groups: those in group A possess A antigens and B antibodies, those in group B have B antigens and A antibodies, those in group AB contain both antigens but lack antibodies, and those in group 0 lack antigens but have both types of antibodies. In 1939, a blood factor labelled Rh was discovered in rhesus monkeys, which was later found in humans. The essential factor in the Rh system is the D antigen. About 85% of humans have this factor on the surface of their red blood cells and are Rh-positive (Rh+), and the rest are Rh-negative (Rh-). Depending on the presence or absence of this factor in each basic blood group, people fall into eight groups: A(2)-positive; A(2)-negative; B(3)-positive; B(3)-negative; AB(4)-positive; AB(4)-negative; 0(1)-positive; 0(1)-negative [11]. The most common blood groups are A and 0, and B and AB are rarer.

Blood group antigens can be identified not only on erythrocytes, but also on leukocytes, some tissues, platelets, cell surface enzymes, and in fluids such as saliva, sweat, urine, gastric secretions, breast milk, seminal and amniotic fluid, etc. It appears that most of these antigens are the product of a single gene, which has undergone mutations (such as deletions, inversions, insertions), alternative splicing, single-nucleotide polymorphisms (SNPs), etc., which can give rise to new antigens or the loss of their expression. Glycoconjugate structures on erythrocytes can also

function as ligands for microorganisms, parasites, and various molecules (structural proteins and enzymes, adhesive molecules, transporters etc.) [12].

Returning to the link between blood type and certain human traits, it is generally considered that people with type 0 are phlegmatic (relaxed and pacifistic), those with type A are melancholic (self-sufficient/deep thinkers), those with type B are sociable and extroverted, and those in group AB (rarer), are confident, sociable, but at the same time shy, do not demand attention or use excuses, have very good logical and analytical skills, can be perceived as irresponsible, self-centred, indecisive, vulnerable, forgetful, critical and unforgiving. A breakdown of individual traits specific to each blood group would have the following picture:

- ▶ Blood group 0 individuals are responsible and cautious and choose the safe option, not the spontaneous one. They are seen as trustworthy but predictable, which some do not appreciate. They are unwilling to do things differently, making them appear stubborn. They are sociable, fear nothing, and want to move forward. They do their best to achieve their goals, are natural leaders, and prefer to focus on the big picture. They are strong and can endure even the most difficult situations. They prefer honesty and resent it when others lie. At the same time, some may consider them to be jealous, rude, cold, and ruthless. Their traits include optimism, confidence, resilience, and self-determination.
- ➤ Blood type A they think deeply and are self-confident. At the same time, they are rational and controlled and live life according to their formula. They prefer harmony and are patient and loyal, but are more sensitive to certain aspects of life than other groups. They can be adamant about etiquette and social norms, don't like to rush when it comes to making decisions, and don't like multitasking. They want to keep things in order and plan their tasks rigorously. They can be stubborn and easily stressed, which may be due to high levels of the stress hormone cortisol. They don't put up with drama, follow the rules, and do only what is necessary. They have self-confidence, which can qualify them as snobbish in the eyes of others. *The basic traits of* people with blood type A are cleverness, sensitivity, kindness, shyness, attentiveness, and stubbornness. They are passionate, cooperative, reliable, and perfectionists.
- ➤ Blood type B passionate, creative, quick decision-makers, can't stand taking orders, but get totally involved when they set their mind to something, whether it's their personal or professional life, for them it's "all or nothing". They want to be the best in their field, but can't bear to multitask. They prefer to let other vital tasks slide when trying to achieve a goal. They are relaxed, adventurous, outgoing, curious and cheerful. They can be stubborn, selfish, and uncooperative.
- ➤ **Blood type AB** are considered people with leadership traits. They are confident and sociable, but at the same time shy, not attention-seeking, and do

not use excuses. When they have specific goals, they do everything to achieve them. When they are around strangers, they may hide their ways. They are empathetic and caring when interacting with others. They have excellent logical and analytical skills. They can be seen as irresponsible, self-centred, indecisive, vulnerable, forgetful, critical, and unforgiving. Individuals with this blood type are adaptable and calculating but tend to be indecisive. They are sometimes introverted and do not let others into their lives.

Individuals with blood group AB have a unique ability; in the case of blood transfusions, they are universal recipients, while those with blood group 0 are universal donors. According to studies, people with blood type AB excel at multitasking and can complete any task quickly. They have high standards and prefer to be treated with care by those around them [13-18].

An individual's blood type does not change throughout life. Blood groups are an essential feature of human biology, an important element that defines us, and significantly influence our health. The AB0 and Rh systems are crucial to medical altmetrics, allowing the determination of the eight blood groups. The other systems are of practical importance only in cases of paternity.

Knowledge of blood group and Rh is essential in determining cases of incompatibility in blood transfusion. The Rh system must also be considered in the case of pregnancy (when the child differs in Rh from the mother). Forty-five proteins have been identified as part of the Rh system, the most common of which is protein D (D antigen).

The presence or absence of the Rh factor is important in medical Haematology for at least two reasons:

- ➤ To avoid the process called *haemolysis* (foetal erythroblastosis). If an Rh-person receives a transfusion from an Rh+ person, anti-Rh antibodies develop in the blood of the person receiving the transfusion, which destroys the red blood cells in the transfused blood when a second transfusion is given.
- Rh incompatibility is also crucial in pregnancy: if the mother is Rh-negative and the foetus is Rh+, and in the first pregnancy does not receive treatment to prevent the formation of anti-Rh antibodies, in a second pregnancy of the same type, the anti-Rh antibodies will destroy the baby's red blood cells, which can lead to severe anaemia and in some cases even death.

The Rh-negative blood group can donate blood to both Rh blood groups, but the Rh-positive blood group can donate only to the Rh-positive blood group. **Rh-negative** group **0** is a universal donor.

The Rh factor must be determined in the following situations: before a transfusion; before a surgical intervention that might require transfusions; in case of pregnancy, when immuno-hematologic and postnatal monitoring of the mother and child is necessary.

In Romania, the distribution of blood groups is as follows: group OI 34%, group AII 41%, group BIII 19%, and group ABIV 6% (Table 7).

Table 7. Distribution of blood groups by AB0 and Rh system

Country	Population	<i>O</i> +	A+	B+	AB+	<i>O</i> -	A-	В-	AB-
Romania	21.302.893	28%	37%	14%	7%	5%	6%	2%	1%

Blood group compatibility taking into account the AB0 and Rh system (Table 8).

Table 8. Distribution of blood groups by the AB0 and Rh system

Blood type	Can donate to	Can receive from
0+	O+ A+B+AB+	0+ O-
A+	A+ AB+	A+ A- O+O-
B+	B+ AB+	B+ B- O+ O-
AB+	AB+	ALL
O-	ALL	O-
A-	A+ A- AB+ AB-	A- O-
B-	B+ B- AB+ AB-	B- O-
AB-	AB+ AB-	AB- A- B- O-

In medical altmetry, it is imperative to know the blood group. It can, for example, facilitate the transfusion process by reducing the control time. The patient's blood group is determined before a surgical procedure with a potential risk of a bleeding complication, which would require a blood transfusion. Some authors have tried to determine whether there is a link between blood group and susceptibility to certain diseases and pathogens. Such information, summarised by Abegaz (2021) [12], shows that:

- people with group AB (regardless of area, race, age, and gender) would have a higher risk of contracting cognitive impairment, higher incidence of smallpox, colic bacillus, and salmonella infections;
- those with blood group 0 would have an increased incidence of cholera, plague, tuberculosis, and salmonella infections;
- those with blood group A would be more susceptible to smallpox and *Pseudomonas aeruginosa* infections;

– Blood group B would be associated with a higher incidence of infections with *Neisseria gonorrhoeae*, *Streptococcus pneumoniae*, and *Salmonella*. Also, individuals with blood group A would be more susceptible to cancers of the stomach, ovaries, salivary glands, uterus, and colon than those with blood group 0. There would also be a relationship between the AB0 system, thromboembolic diseases, and the risk of bleeding, involving glycosyltransferase and coagulation factor VIII levels (which are lower in group 0). The author concludes, however, that in the AB0 system, it is not clear whether blood group can be the cause of disease, but rather that it can facilitate susceptibility to specific health problems and that, in general, groups A, B, and AB are more susceptible than group 0.

In a study involving more than 400 thousand subjects of blood groups 0, A, and B (group AB was not considered due to a small number of carriers), Groot, (2020) [19] observed that in contrast to group 0 individuals, those in groups A and B are more susceptible to thromboembolic phenomena and have a lower risk for hypotension. As reported by Gilmiyarova et al, (2020) [20] blood group 0(I) carriers would be more resistant to diseases (except gastrointestinal diseases), while those in groups A(II), B(III), and AB(IV) would be more prone to infections and to the development of cancers and cardiovascular diseases. Finally, a more cautious view, and probably a correct one, is held by Amjadi et al (2015) [21], who show that investigations focused on this topic have reached contradictory results, that blood groups in the AB0 system do not cause diseases. However, their presence influences susceptibility and disease resistance, so carriers of blood groups A, B, and AB are generally more susceptible than group 0. Such studies are still needed, as knowledge of health risks according to blood group contributes to identifying measures to counteract them by changing lifestyle, habits, health, and environmental behaviour, a view supported by other authors [22-30].

AB0 system agglutinogens

Figure 1 shows the scheme of antigen formation. Four steps are differentiated as follows:

- **a.** A basic mucopolysaccharide substrate (linear or branched oligosaccharides) is modified, under the action of the **H** gene, by the addition of an L-fucose molecule, resulting in **substance H**, or **the antigen H**, common to A and B. Note that the mucopolysaccharide substrate is similar in structure to a pneumococcal antigen. The H gene encodes a *glycosyltransferase* required to synthesise both **A** and **B**;
- **b.** If the A gene is present in the genotype, it causes the synthesis of a glycosyltransferase, which causes an *N-acetyl-galactosamine* residue to be attached to the H substance, resulting in the **A** antigen.

- **c.** If the B gene is present in the genotype, it causes the synthesis of a glycosyltransferase which attaches a *D*-galactose residue to substance H, resulting in antigen **B**.
- **d.** If the genotype contains both A and B genes, the relationship between them is one of *codominance*, the resulting phenotype showing both agglutinogens in approximately equal amounts, i.e., blood group AB.

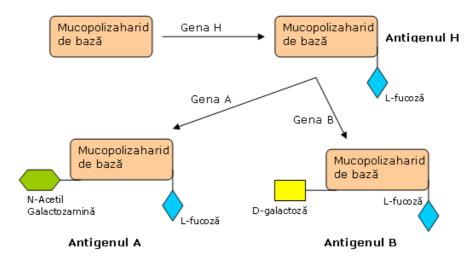


Fig. 1. Scheme of antigen formation [31]

AB0 system agglutinins

Agglutinins are antibodies (gamma-globulins, immunoglobulins) belonging to the IgM and IgG classes, sharing a common structure and origin. They are primarily of the IgM type, also known as hemagglutinins or isohemagglutinins. Their titre is nearly undetectable at birth and becomes measurable around six months. Their levels rise steadily until 8-10 years of age when they reach a titre that will be maintained throughout adult life. They decline in old age but do not disappear. How an organism that has never come into contact with AB0 antigens synthesises these antibodies is still uncertain.

Genetics of the AB0 system

The inheritance of the four basic blood groups of the AB0 system is under the control of three genes placed at the same locus on the long arm of human chromosome 9 (9q34) -LA, LB (codominant), and 1 (recessive). In other papers, these genes are denoted IA, IB and I, respectively. Due to codominance, the presence of the LA and LB genes in the same genotype gives rise to the AB phenotype (blood group). Phenotypes (blood groups) A, B, AB and 0 can have the following genotypes: group

A – genotypes LALA or LAI; group B – genotypes LBLB or LBI; group AB – genotype LALB, and group 0 – genotype ll. Below (Table 9) are the blood groups of children born to parents with different blood groups [11].

Parents		Children	
Blood type	Genotype	Possible	Impossible
AxA	L ^A l x L ^A l	A, 0	B, AB
BxB	$L^{B}l \times L^{B}l$	B, 0	A, AB
AB x AB	$L^{A}L^{B} \times L^{A}L^{B}$	A, B, AB	0
0 x 0	11 x 11	0	A, B, AB
AxB	$L^{A}l \times L^{B}l$	A, B, AB, 0	-
A x AB	L ^A l x L ^A L ^B	A, B, AB	0
A x 0	L ^A l x ll	A, 0	B, AB
B x AB	$L^{B}l \times L^{A}L^{B}$	A, B, AB	0
B x 0	L ^B l x ll	B, 0	A, AB
AB x 0	L ^A L ^B x ll	A, B	AB, 0

The l allele is recessive and occurs only in the homozygous state, with the ll genotype determining blood group O, characterised by the presence of the unmodified H antigen on the erythrocytes [32-38].

Other blood antigen systems

There are numerous other antigen systems on figurative blood elements. The number of possible phenotypes considering all these systems is in the order of billions. Moreover, the immune system eventually destroys the cells that enter the body during a transfusion within 7-10 days, making it virtually impossible to obtain complete identity between donor and recipient phenotypes. Table 10 shows the most widely known blood antigen systems [32-38].

Table 10. Blood antigen systems

No.	Classical name	Notation (abbreviation)	Nature of epitope (antigenic determinant)	Localisation on chromosome
01	AB0	AB0	N-acetylgalactosamine, galactose	9
02	MNS	MNS	GPA / GPB (glycophorins A and B)	4
03	P	P1	glycolipid	22
04	Rhesus	Rh	protein	1
05	Lutheran	Lu	IgSF (protein, immunoglobulin)	19
06	Kell	Kel	glycoprotein	7

07	Lewis	LE, Le	fuse	19
08	Duffy	Fy	protein (ECR, chemokine receptor, Plasmodium vivax and knowlesi receptor)	1
09	Kidd	JK	protein (urea transporter)	1
10	Diégo	DI	glycoprotein ('band 3 protein', AE 1, ion transporter)	17
11	Cartwright	YT	protein (AChE, acetylcholinesterase)	7
12	Xg	XG	glycoprotein	X
13	Scianna	SC	glycoprotein	1
14	Dombrock	DO	glycoprotein (bound to the membrane by glycosylated phosphatidylinositol – GPI)	12
15	Colton	CO	aquaporin 1	7
16	Landsteiner- Wiener	LW	IgSF (protein, immunoglobulin)	19
17	Chido/Rodgers	Ch/Rg	C4aC4b (complement fractions)	6
18	Hh	Н	fuse	19
19	Kx	XK	glycoprotein	X
20	Gerbich	Ge	GPC / GPD (glycophorins C and D)	2
21	Cromer	Cro	glycoprotein (DAF or CD55, regulator of complement C3 and C5 fragments, membrane-bound by glycosylated phosphatidylinositol)	1
22	Knops	Kn	glycoprotein (CR1 or CD35, Ag-Ac complex-binding)	1
23	Indian	In	glycoprotein (CD44, a possible adhesion protein)	11
24	OK	OK	glycoprotein (CD147)	19
25	RAPH	MER2	transmembrane glycoprotein	11
26	John Milton Hagen	ЈМН	protein (membrane-bound via phosphatidylinositol glycosylate)	6
27	Ii	I	branched (I) or unbranched (i) poliovirus	6
28	globoside	P	glycolipid	3
29	GIL	GIL	aquaporin 3	9
	1		<u> </u>	

Patient biorhythm

Another altmetric characteristic of a patient is related to biorhythm. It is known that those who are born after 1.00 a.m. until 12.00 p.m. are early risers, get up early in

the morning and do not feel tired, if they have gone to bed by 9.00 p.m. and have their regular work schedule between 8.00 a.m. and 2.00 p.m., with the maximum intellectual output at 10.00, and people born between 12.00 and 24.00 are late, cannot get up until 8.00, appear tired earlier, and have their regular work schedule between 10.00 and 20.00, with the maximum intellectual output after 16.00.

Conclusions

This paper presents some current aspects of medical altmetrics used as a precursor in Artificial Intelligence (AI). Modern methods of medical analysis in a system of digitisation, co-authorship, and corroboration between interdisciplinary techniques are involved in assessing a patient's health status.

When discussing medical analysis, altmetrics allow for the complete interpretation of results based on the context of clinical information, always focusing on the patient with their suffering or ailment and not on the disease in general. In other words, the patient manages explicitly the course of their suffering. Moreover, the recommended treatment must consider many factors, particularly endogenous factors (blood group, genetic inheritance, static and dynamic biometric characteristics – weight, height, age, immune system, resistance to allergens, etc.). We are discussing the altmetrics of medical analyses to validate only those acuities specific to an integrated patient's suffering. Moreover, several methods are neither standardised nor approved by the competent national agencies (RENAR), and the reference range for the values obtained is not specific to a sick person but to a disease. Thus, the field of biochemical. haematological, immunological, serological, bacteriological, virological, mycological, parasitological, histological, cytological, pathological and other types of investigations by examining samples from the human body (blood specimens, urine, CSF, secretions, tissues, etc.), as well as from the field of imaging or functional explorations are taken into consideration. They are standardised by accreditation-attestation systems of quality and conformity of characteristics, which are unanimously accepted worldwide.

Particular attention is paid to the determination of blood group by the AB0/Jan Jansky system and the Rhesus (Rh) factor, which has both a medical and personal importance, being linked to the risk of developing certain diseases (coronary pathologies, gastric cancer, peptic ulcer, memory, thinking and reasoning problems, associated with dementia, etc.) and which provides essential information to specifically guide lifestyle, intending to reduce the risk of developing certain associated health conditions.

In all testing/analysis approaches, but also in researching difficult diagnostic cases to establish a treatment, a specific Artificial Intelligence algorithm is developed (e.g., AB0 testing algorithm, Rhesus membership research algorithm in challenging diagnostic cases, immune-haematological investigation algorithm, etc.). The family history or health history of first-degree relatives and the patient's biorhythm will also be considered in diagnosis and treatment.

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