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Evaluation of Physicochemical Properties of Some Orthodox Antimalarials Used In South –East, Nigeria.

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Abstract

Oral bioavailability of drug is determined by its physicochemical properties which governs its rate limiting release at the gastrointestinal tract for absorption into the systemic circulation. We conducted pilot study of physicochemical properties (colour, size, molecular weight, dissolution time, pH solubility and specific gravity) of few selected antimalarial agents of 2 to 5 different brands (trade name), but the same generic from 4 different makes. Our pilot study showed variability in physicochemical properties, both intra and inter differences. The need, therefore, to maintain good clinical pharmacological practice to ensure safety and potency of antimalarial agents and to prevent Plasmodium parasite resistance.

Keywords: Evaluation, Physicochemical properties, Antimalarial agents.

Introduction.

Oral bioavailability of a drug is determined by a number of its properties, including drug dissolution rate, solubility, molecular weight, pH, size. These factors govern intestinal permeability and pr-systemic metabolism that lead to achieving desired concentration at the target site (Jambkekar and Breen, 2013). More often than not, the rate limiting step in drug absorption from the gastrointestinal tract is drug release and drug dissolution from dosage form. Therapeutic agents with aqueous solubility less than 100µ/ml often present dissolution limitations to absorption. The pk_a of a drug in relation to the gastrointestinal pH profile also determines solubility of a drug in the gastrointestinal fluid contents (Jambkekar and Breen, 2013). Physicochemical, formulation-related and physiological factors can all influence drug dissolution and ultimately limit drug bioavailability and desired concentration at the target site. For many drugs, pharmacological response and therapeutic effectiveness is related to observed blood concentration. Drug concentration at the target site is largely dependent on blood bioavailability which reflects physicochemical properties and metabolism. However, this assumption does not hold true in all cases. This is not always the case in oral drug administration where the site infection may be far from the gastrointestinal tract (Jambkekar and Breen, 2013). In situations such as this, other approaches are employed to achieve the desired response. In spite of these limitations, bioavailability remains the only parameter to assess the rate and extent of drug absorption and suggest implication of drug formulation. Drug dissolution and drug absorption processes and their consequential effects on bioavailability appear to be interdependent processes that are influenced by the physicochemical properties of drugs, in particular hydrophobic drugs, (Molavi *et al*.,2021). Understanding the intricate interplay of physicochemical properties stands as a pivotal factor influencing the uncertain balance between a drug's pharmacokinetic and pharmacodynamic profile. Oral bioavailability of a drug is the product of fraction of drug absorbed, fraction of drug escaping intestinal metabolism and fraction of drug escaping liver metabolism (Molavi *et al*.,2021). Therefore, oral bioavailability of a drug is largely a function of its solubility

characteristics in gastrointestinal fluids, absorption into the systemic circulation and metabolic stability (Stielow *et al*.,2023).

Hence, oral absorption and the fraction of drug absorbed into the intestine are functions of drug solubility and permeability (Dahan and Miller, 2012). These properties emerge as cornerstones, driving the potential to elevate the triumph of drug candidate in achieving clinical response. Impaired solubility, stability (pH), dissolution (weight and size) can affect permeability resulting in diminished absorption within gastrointestinal tract, and subsequently leading to a decline in oral bioavailability. This may hinder the effectiveness of a drug and its ability to attain the necessary exposure levels crucial for its intended purpose (Lu *et al.,* 1993; Ramteke *et al*., 2014). This work wants to reflect the overall importance of these properties in contributing to the success or failure of a potential therapeutic agent in resolving clinical cases.

Materials and method

Ten antimalaria blisters containing various numbers of tablets commonly used in Enugu and Ebonyi states and their environs were randomly bought at registered ten pharmaceutical stores serving the public. The antimalarial agents used for the study were grouped into three, in tandem with their chemical composition similarities. Each group has the same mechanism of action (of the same generic) on malaria parasite but from different makes. The authenticity of each blister and tablets inside and expiry dates were well ascertained and assured. Their generic names are: The physicochemical properties evaluated were: colour, size, molecular weight, dissolution time, solubility, pH, and specific gravity.

Result

Table 1: Baseline characteristics of the study antimalarial agents

S/N	Generic name	Colour	Size (cm)	Molecular weight(mg)	Dissolubility (minutes)	Solubility	pH
1	Sulphadoxine 500mg+pyrimethamine25mg	White	1.3	700	11	Soluble with fine crystal	6
2	Sulphadoxine 500+pyrimethamine 25mg	White	1.6	600	18	The same as above	6
3	Artemether 80mg/lumefantrine400mg	Yellow	1.6	800	55	As above	6
4	Artemether 20mg/lumefantrine 120mg	White	1.0	300	47	As above	7
5	Artemether 20mg/lumefantrine 120mg	Yellow	1.1	200	50	Not soluble	6
6	Artemether 20mg/lumefantrine 129mg	Yellow	0.9	400	22	As above	6
7	Dihydroartemisinin 30mg/piperaquine phosphate 225mg	Milky white	1.1	600	11	As above	4.5
8	Artemisinin 62.5mg/piperaquine 375mg	Sky blue	1.3	600	22	As above	5.0
9	dihydroartemisinin 40mg/piperaquine phosphate 320mg	Light green	1.6	500	60	Soluble	6

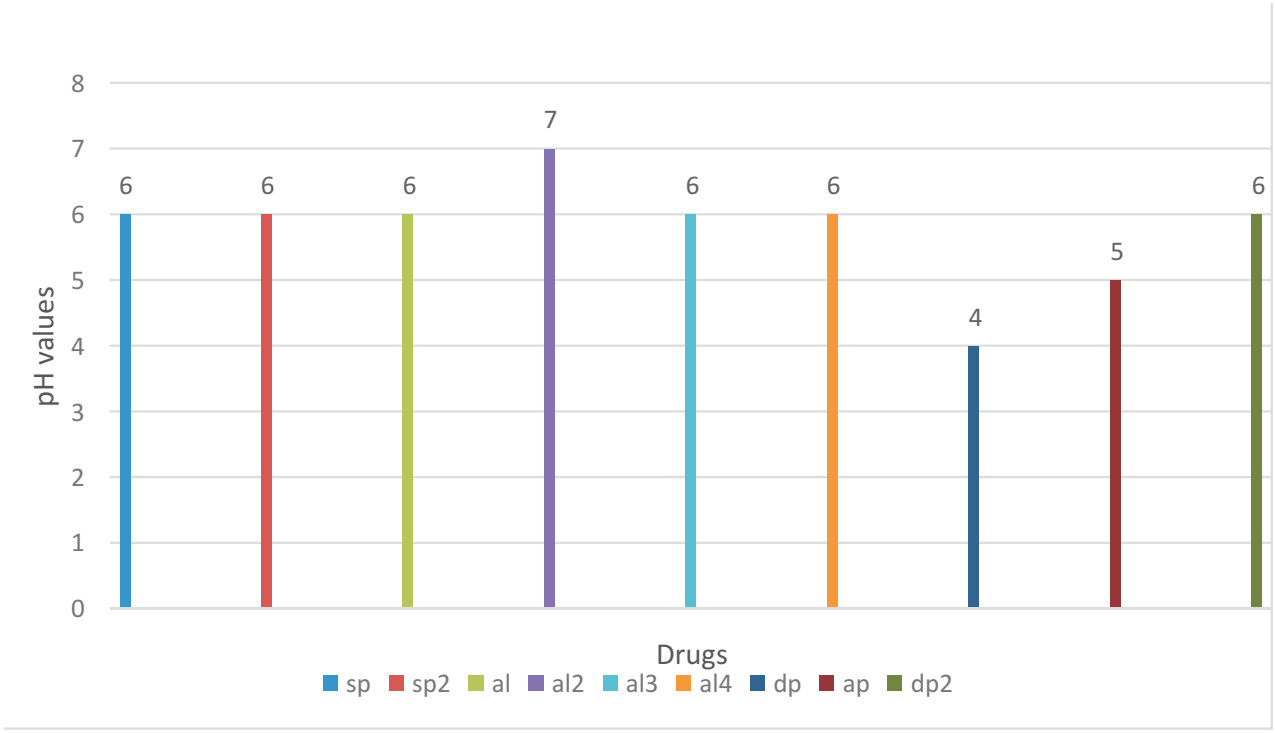

Figure 1: Antimalarials and their pH
Key:
sp- Sulphadoxine 500mg +pyrimethamine 25mg
al- arthemether + lumefantrine
dp- dihydroartemisinin + piperaquine
ap- artemisinin + piperaquine

The result of the baseline characteristics of the study antimalarial agents commonly used for the treatment of uncomplicated malaria in East-Nigeria are shown in Table 1. Figure 1 shows the pH of each drug.

Discussion

The physicochemical properties (size, molecular weight, dissolution time, solubility, pH and specific gravity} of therapeutic agent predetermine the rate and extent at which the administered dose of the agent reaches the general circulation (Ramteke *et al*.,2014). For many drugs that cross intestinal mucosa easily the onset of drug levels will be controlled by the time required for the dosage form to dissolve and release its content to the target site.

Dissolution is a process by which a solid substance dissolves in a medium and is a fundamental property of a solid drug. Equilibrium solubility of a drug is the major determinant of its dissolution rate, particularly for problematic poorly soluble and hydrophobic drugs. The drug might be considered poorly soluble when its dissolution rate is slower than the time it takes to transfer past its absorption sites, resulting in incomplete bioavailability. This generally, is the case for drugs where aqueous solubility is less than 100μg/ml (Hörter and Dressman, 2001).

Solubilization which has been defined as the preparation of a thermodynamically stable solution of a substance that is normally insoluble or very slightly soluble in a given solvent can be made soluble by incorporation of surfactant or bile salt to form micelles and therefore, made soluble for poorly soluble drugs (Jin *et al.*, 2021). Our work showed that most of the test drugs dissolved between 11 and above 60 minutes and one of the drugs did not dissolve completely after 60 minutes. Two of the test drugs dissolved completely in a very short period of 11 and 20

minutes. Seventy percent of the 9 tested drugs dissolved, though with crystals. One of the drugs dissolved slowly for over 50 minutes but with complete solubility. The variability in dissolution time, we hypothesized might undermine their activities even to sensitive species. The sizes of the study drugs ranged between 0.9 and 1.6cm and molecular weight of 20mg/ml and 70mg/ml. This significant difference in molecular weights (20-70mg) will present different dissolution challenges and variability in bioavailability. Particle size and molecular weight have direct correlation with surface area. Therefore, therapeutic agents in powder formulation have larger surface area than those with large particle size and large molecular weight. Earlier report showed that dissolution rate is directly proportional to the surface area of powder formulation (Jambhekar and Breen, 2013).

Therapeutic agents with aqueous solubility less than 100µg/ml often present dissolution limitations for absorption (Jambkekar and Breen, 2013). Solubility in the gastrointestinal fluid contents is determined by aqueous solubility, crystalline form, drug lipophilicity, solubilization and pka of a drug in relation to gastrointestinal pH profile (Hörter and Dressman,2001; Gaohua *et al*., 2021).

The pH of our test - drugs showed wide degree of difference (4.5-7.0) in distilled-deionized water. These properties affect the dissolution, absorption and bioavailability of drugs to systems. Largely, bioavailability of drug is a product of a fraction of drug absorbed, a fraction of drug escaping intestinal and liver metabolisms (Varma *et al.,* 2010). Historically, physicochemical properties concept of orally formulated therapeutic agents for a common therapeutic response should be closely related if not exclusively. Therefore, all factors that influence drug dissolution will probably influence drug absorption and, therefore bioavailability, (Molavi *et al*.,2021). However, our work did not extend to investigation of activities of the few selected antimalarials studied as a function of the physicochemical properties, but our hypothesis here is that clinically improper manipulation of physicochemical properties of a drug will render it ineffective for its intended purpose.

Conclusion: The above discussion clearly illustrates variability in physicochemical properties (size, weight, pH, dissolution time and solubility) of some selected antimalarial agents, as factors that are known to affect bioavailability and drug concentration at the target site. Therefore, there is need to maintain good clinical pharmacological practice to safe existing antimalarials from being over-overwhelmed by malaria parasite strain.

References

Dahan, A., Miller, J.M. (2012). The solubility-permeability interplay and its implications in formulation design and development for poorly soluble drugs. *American Association of Pharmaceutical Scientists*;**14(2)**:244-251.

Gaohua, L., Miao, X. and Dou, L. (2021). Crosstalk of physiological pH and chemical pKa under the umbrella of physiologically based pharmacokinetic modeling of drug absorption, distribution, metabolism, excretion, and toxicity. *Expert Opinion On Drug Metabolism & Toxicology*;**17(9)**:1103–1124.

Hörter, D., Dressman, J.B. (2001). Influence of physicochemical properties on dissolution of drugs in the gastrointestinal tract1PII of original article: S0169-409X(96)00487-5. *Advanced Drug Delivery Reviews*; **46(1–3)**: 3: 75-87.

Jambhekar, S.S., Breen, P.J. (2013). Drug dissolution: significance of physicochemical properties and physiological conditions. *Drug Discovery Today*; **18(23–24)**: 1173-1184.

Jin, G, Ngo, H.V., Cui, J.H., Wang, J., Park, C., Lee, B.J. (2021). Role of Surfactant Micellization for Enhanced Dissolution of Poorly Water-Soluble Cilostazol Using Poloxamer 407-Based Solid Dispersion via the Anti-Solvent Method. *Pharmaceutics*;**13(5)**:662.

Lu, A.T.K., Frisella, M.E. & Johnson, K.C. (1993). Dissolution Modeling: Factors Affecting the Dissolution Rates of Polydisperse Powders. *Pharmacy Research;* **10:** 1308–1314.

Molavi, F., Hamishehkar, H., Nokhodchi, A. (2020). Impact of Tablet Shape on Drug Dissolution Rate Through Immediate

Released Tablets. Advanced Pharmacy Bulletin;**10(4)**:656-661.

Ramteke K.H., Dighe P.A., Kharat A.R., Patil S.V. (2014). Mathematical Models of Drug Dissolution: A Review. *Scholars Academic Journal Of Pharmacy* (SAJP); **3(5)**: 388-396.

Stielow, M., Witczyńska, A., Kubryń, N., Fijałkowski, Ł., Nowaczyk, J., Nowaczyk, A. (2023). The Bioavailability of Drugs-The Current State of Knowledge. *Molecules*;**28(24)**:8038.

Varma, M.V., Obachm, R.S., Rotter, C., Miller, H.R., Chang, G., Steyn, S.J., El-Kattan, A., Troutman, M.D. (2010). Physicochemical space for optimum oral bioavailability: contribution of human intestinal absorption and first-pass elimination. *Journal of Medicinal Chemistry*;**53(3)**:1098-108.

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