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Assessment of Human Pharmaceutical Products Registered in Kenya by Route of Administration and Type of Dosage Form

N.N. NYAMWEYA* and L.J. TIROP

Department of Pharmaceutics and Pharmacy Practice, School of Pharmacy, College of Health Sciences, University of Nairobi, P.O. Box 19676-00202, Nairobi, Kenya.

The aim of this study was to assess the human pharmaceutical products that have been registered in Kenya in order to determine the most common routes of administration and type of dosage forms that are used. Registered pharmaceutical products were categorized by route of administration and then sub-categorized by the dosage form. Oral dosage forms were the most common accounting for 73% of all registered products. Parenteral and topical products represented 18% and 4% of the registered products respectively. Ophthalmic and pulmonary dosage forms accounted for 2% and 1% of the registered products, respectively. All other dosage forms categories individually accounted for less than 1% of the registered products. For most routes of administration, a variety of specific dosage forms were observed. The paper also briefly reviews the advantages and disadvantages of the routes of administration and the dosage forms that were observed.

Keywords: Route of administration, dosage forms, drug delivery, registered pharmaceutical products

INTRODUCTION

Medicinal agents (active pharmaceutical ingredients) given to patients are introduced into the body by a particular route of administration. Each route of administration has associated advantages and disadvantages. Additionally, for any given route of administration, it is possible that the medicinal agent may be formulated in more than one dosage form. A dosage form may be defined as the vehicle which is used to deliver the drug into the body. The term "drug" would then refer solely to the medicinal agent (i.e., the active pharmaceutical ingredient {API}). For example, an API may be given orally or intravenously which would represent two different routes of administration. Furthermore, the API may be available commercially as a solid (e.g., tablet) or as a liquid (e.g., syrup) product which would represent two different dosage forms.

While it is widely known that oral dosage forms are the most common dosage forms available, there is a paucity of published data which actually indicate the proportion that oral products represent in specific pharmaceutical markets.

Knowledge of the dosage forms available in a given market is important for a number of reasons. For academics, this information is required so that educational programs will cover the products that are commercially available. Healthcare professionals need to be aware and have up to date information on the various types of dosage forms that are available in the region in which they practice. For pharmaceutical manufacturers, this information may be used in market research and to identify areas where there is an unmet need in terms of drug delivery. For pharmaceutical regulatory authorities, knowledge of available dosage forms can help guide drug regulation and surveillance programs, and future drug registration.

A review of the literature did not yield any published scientific reports on the dosage

*Author to whom correspondence may be addressed.

forms present in Kenya. However, there are various business reports for certain regions which offer market research information on drug delivery which may have some relevant information in this area. This information, however, is specific to certain markets and is not readily available due to the extremely high cost of these reports and their limited distribution.

The aim of this study was therefore to provide an analysis of the human pharmaceutical products that have been registered in Kenya and categorize them by 1) the route of administration, and 2) the type of dosage form.

EXPERIMENTAL

Information on the type of product was obtained by analyzing the Pharmacy and Poisons Board database of registered human drugs [1]. The products were categorized first by the route of administration and secondly by the type of dosage form. Oral products were first sub-categorized as solids or liquids and then sub-categorized into a specific dosage form. The routes of administration used for categorization were oral, parenteral (injections), topical, ophthalmic, pulmonary, vaginal, otic, rectal, nasal, and transdermal.

RESULTS AND DISCUSSION

Table 1 shows the number of registered products by route of administration. Ninety-four percent of the products registered were classifiable by route of administration. The remainder of the products (e.g., solutions, gels, and sprays) were listed in the database, but could not be correlated to a specific route of administration.

Figure 1 shows the percentages of registered products by their route of administration. Oral dosage forms accounted for the majority of products (73.0%) followed by parenteral (17.7%) and topical (4.2%) products. The high percentage of oral dosage forms results from their patient acceptability, convenience, relative ease of use, manufacturability, and affordable cost (relative to other dosage forms). Solid oral dosage forms (e.g., tablets, capsules and powders) also offer the advantage of product stability (chemical, physical, and microbial).

Table 1: Number of registered products classified by route of administration

Route of administration	Products
Oral	6295
Parenteral	1529
Topical	365
Ophthalmic	159
Pulmonary	82
Vaginal	63
Otic	43
Rectal	42
Nasal	41
Transdermal	2

Figure 2 indicates the distribution of registered products in terms of solid and liquid products. The majority of oral products (83.8%) were solid dosage forms with liquid dosage forms accounting for only 16.2% of oral products. The greater proportion of oral solids can be attributed to their greater stability and portability. Oral liquids, however, do possess certain advantages compared to oral solid dosage forms.

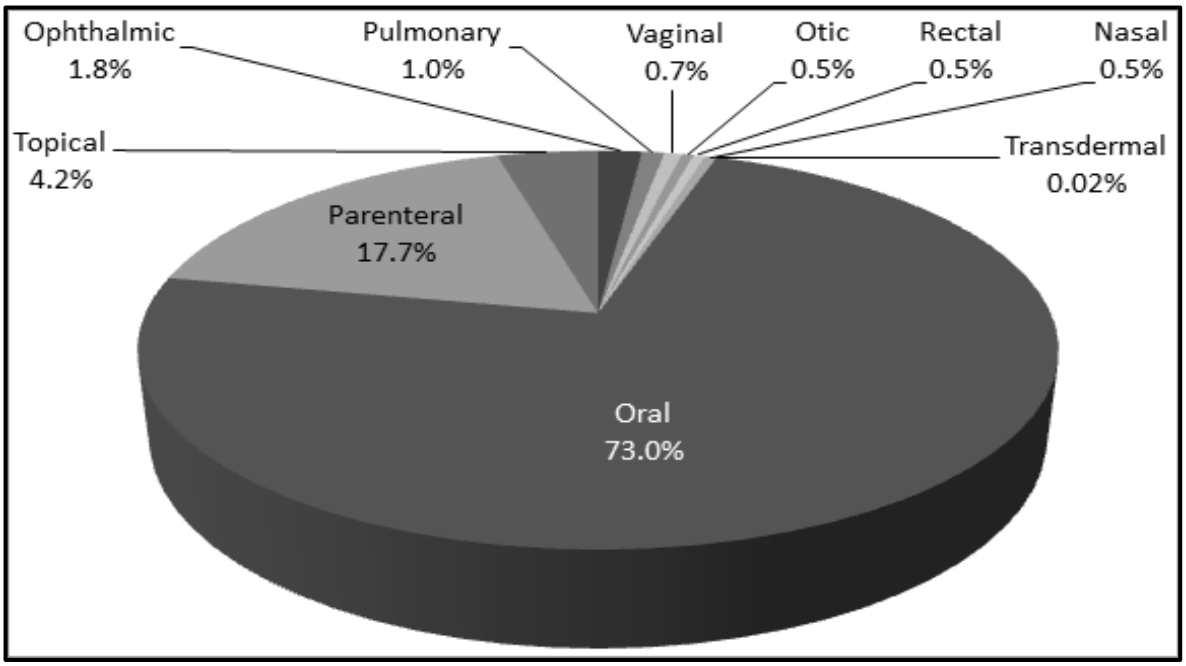

Figure 1. Percentages of registered products by route of administration.

A key advantage is that they are easier to swallow which makes them suitable for patients who have difficulty swallowing conventional solid dosage forms either due to illness or age (e.g., pediatric patients). Liquid dosage forms are commonly utilized for pediatric patients less than five years of age. The extent or rate of drug absorption may be faster for liquid dosage forms because there is no disintegration (solutions and suspensions) step and dissolution (solutions) step, which are prerequisites for drug absorption from solid dosage forms.

The low percentage of oral liquid dosage forms relative to oral solids indeed correlates with a present gap in the Kenyan market. Lack of or scarcity of pediatric oral liquid formulations of essential drugs, such as anti-tuberculosis agents, locally has been reported [2,3]. This gap in age appropriate formulations is often met by compounding of adult solid dosage forms (e.g. crushing of tablets before mixing them with diluents) for administration to pediatric patients. This practice is not always ideal as it is time consuming, may result in inaccurate dosing, and is not suitable for certain drugs (e.g., drugs with stability issues).

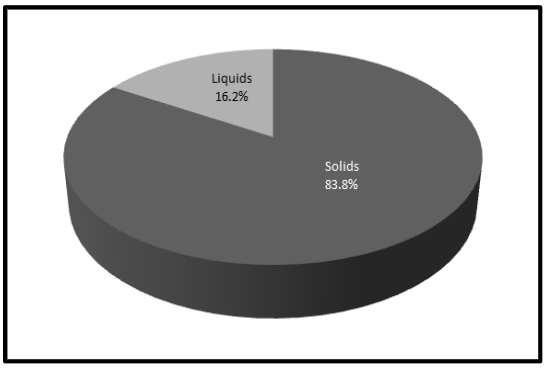

Figure 2. Percentages of registered products listed as oral dosage forms classified as either solid or liquid dosage forms.

The specific types of oral solid dosage forms that were observed for registered products are shown in Figure 3. Tablets and capsules accounted for the majority (76.9% and 20.4%, respectively) of oral solid dosage forms products, respectively. The remaining products (less than 1% each of all oral solid dosage forms) were listed as powders, granules, sachets, dispersible tablets,

chewable tablets, lozenges, dry syrups, or soft gelatin capsules. Sachets indicate a type of packaging usually used for powders or granulations. Tablets are the most popular dosage form because of their broad patient acceptability, portability, and stability as well as their relative ease and very high rate of manufacturing at a comparatively low cost (compared to other dosage forms). Capsules share many of the advantages of tablets (manufacturability, affordable cost, patient acceptability, and portability). Additionally, capsules are easier to swallow than tablets and are tasteless (without a need for coating). Furthermore, capsules can be filled with semi-solids or liquids. Limitations of capsules are their fill volume which limits the dose of drug (since the formulation is not compressed to the same degree as tablets). Another issue that may be observed with capsules is that capsule shells made out of gelatin are susceptible to: 1) physical conditions which alter the amount of water in the shell (e.g., high heat and humidity); and 2) gelatin cross-linking on exposure to certain drugs or excipients. An alternative to tablets and capsules is to use powders (or granules) filled into sachets. The bulkier nature of a powder filled into sachets makes it less portable to carry than tablets or capsules. However, an advantage of powder or granule products is that they can be administered by mixing them with a liquid (or soft food) which facilitates swallowing. The same advantages would also apply to dispersible tablets and dry syrups which have to be reconstituted in a liquid prior to administration. Soft gelatin capsules were listed infrequently and accounted for 0.2% of the oral solid dosage forms. In comparison to hard gelatin capsules, soft gelatin capsules have a thicker shell with a higher amount of plasticizer. They are filled with liquid products or semi-solids which can result in a faster rate of drug delivery if the drug in the fill is dissolved. Soft gelatin capsules are also hermetically sealed due to the manufacturing process which makes them especially suitable for drugs which are liquids, volatile, or sensitive to oxidation [4].

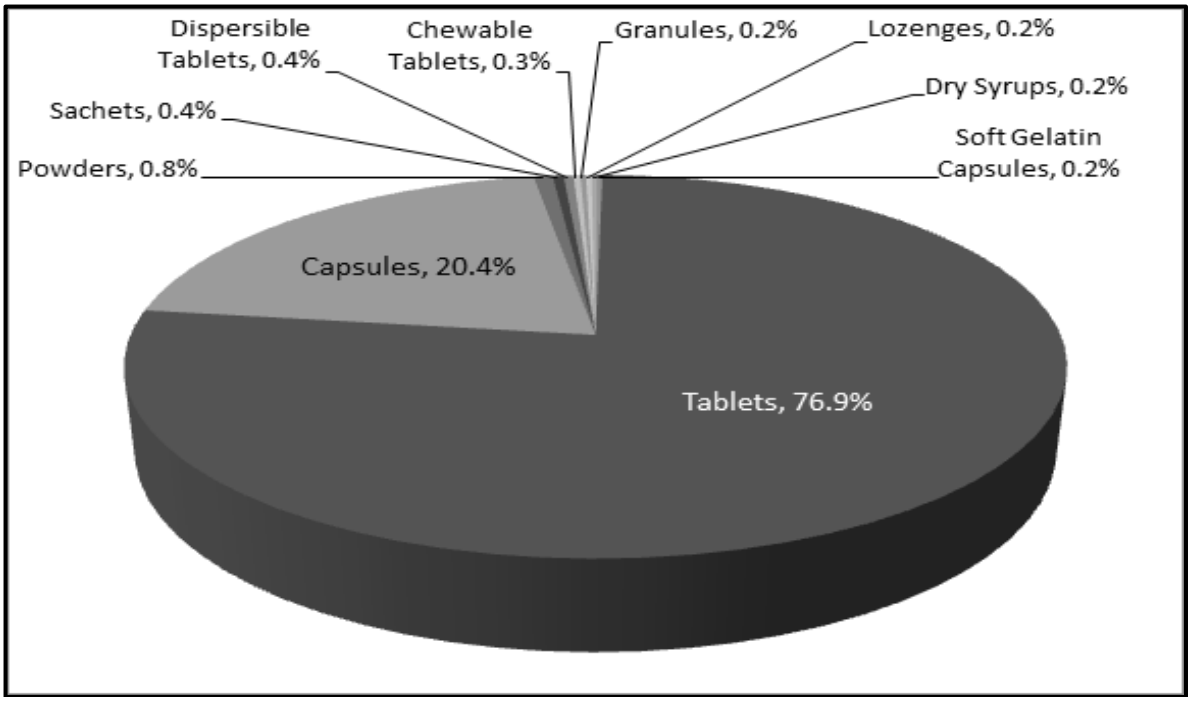

Figure 3. Types and percentages of oral solid dosage forms.

Figure 4 shows the individual types of oral liquid dosage forms that were listed in the database. Suspensions and syrups accounted for the majority (49.9% and 47%, respectively) of the oral liquid dosage forms. Oral solutions, drops, and gels (1.5%, 1.4%, and 0.3%, respectively) accounted for the remainder of the oral liquid products. Oral gels were categorized in Figure 3 as liquids for the purposes of comparison, but technically are more appropriately considered to be semi-solid dosage forms.

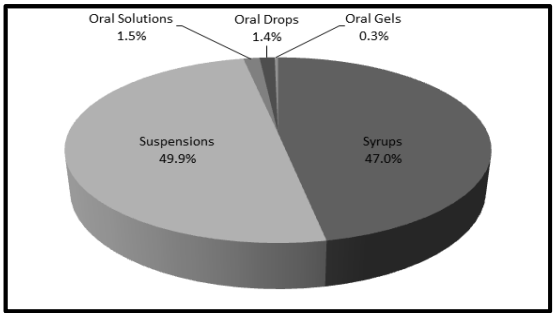

Figure 4. Types and percentages of oral liquid dosage forms.

Figure 5 shows the type and percentage of parenteral products. The registered parenteral products were listed as either injections (94.5%) or infusions (5.5%). The parenteral route is useful when rapid drug delivery is required (e.g., emergencies), oral delivery is not possible (e.g., unconscious patients), and for drugs which are not well absorbed via other routes due to limited absorption or degradation in the gastro-intestinal tract (e.g., biological products). Parenteral dosing also allows very precise control of the amount and rate of drug delivered to the patient. Parenteral dosage forms are usually solutions or (less frequently) emulsions and suspensions. Suspensions are limited to intra-muscular and subcutaneous administration. These products must be sterile which adds to the cost of manufacturing these dosage forms.

There were 67 entries in the database for products listed as vaccines. Most of these are products that would be given by parenteral administration. There were 4 entries for products listed as implants all of which were contraceptives.

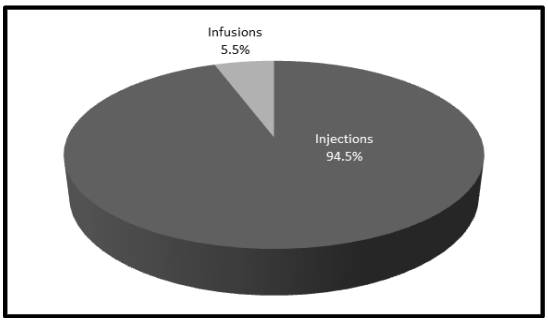

Figure 5. Types and percentages of parenteral products.

The distribution of registered products by route of administration excluding oral and parenteral products is shown in Figure 6. Most drugs administered by these routes (with the exception of the transdermal route and in some cases the nasal and rectal routes) are intended to provide local therapy. This is in contrast to the oral and parenteral routes where the drug delivery produces systemic effects and therefore increases the potential for adverse effects.

The distribution of topical dosage forms for application to the skin is shown in Figure 7. Products in this category would be used to treat dermatological disorders and infections. A major advantage of this route is that the dosage forms used provide local therapy thereby avoiding or minimizing systemic adverse effects. The topical products listed comprised predominantly of creams and ointments (53.5% and 37.4%, respectively). Lotions, powders, and medicated shampoos accounted for the other products (6%, 1.3%, and 1.3%, respectively). There was one product listed as a suspension and one entry for a patch. The single patch in this category was a dermal anesthetic (EMLA® patch [5]). Drug delivery from this patch is considered topical rather than transdermal because the intended therapeutic effect is based on local rather than systemic drug delivery.

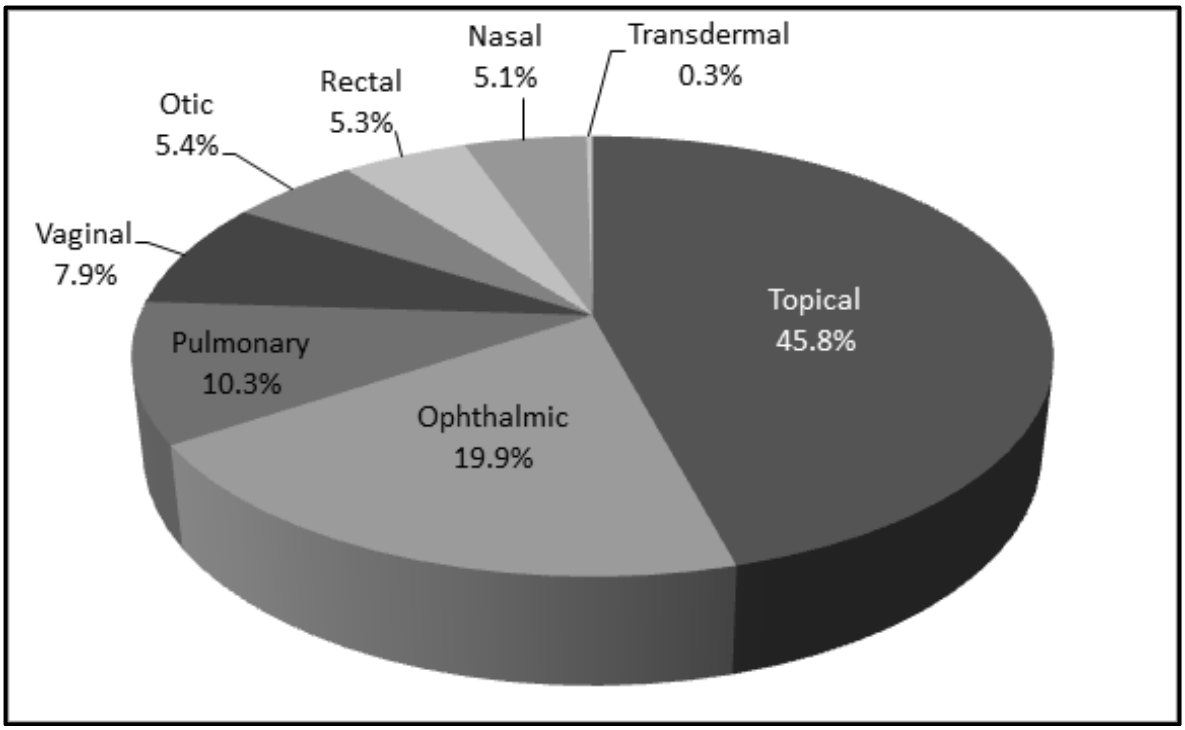

Figure 6. Percentages of registered products by route of administration excluding oral and parenteral products.

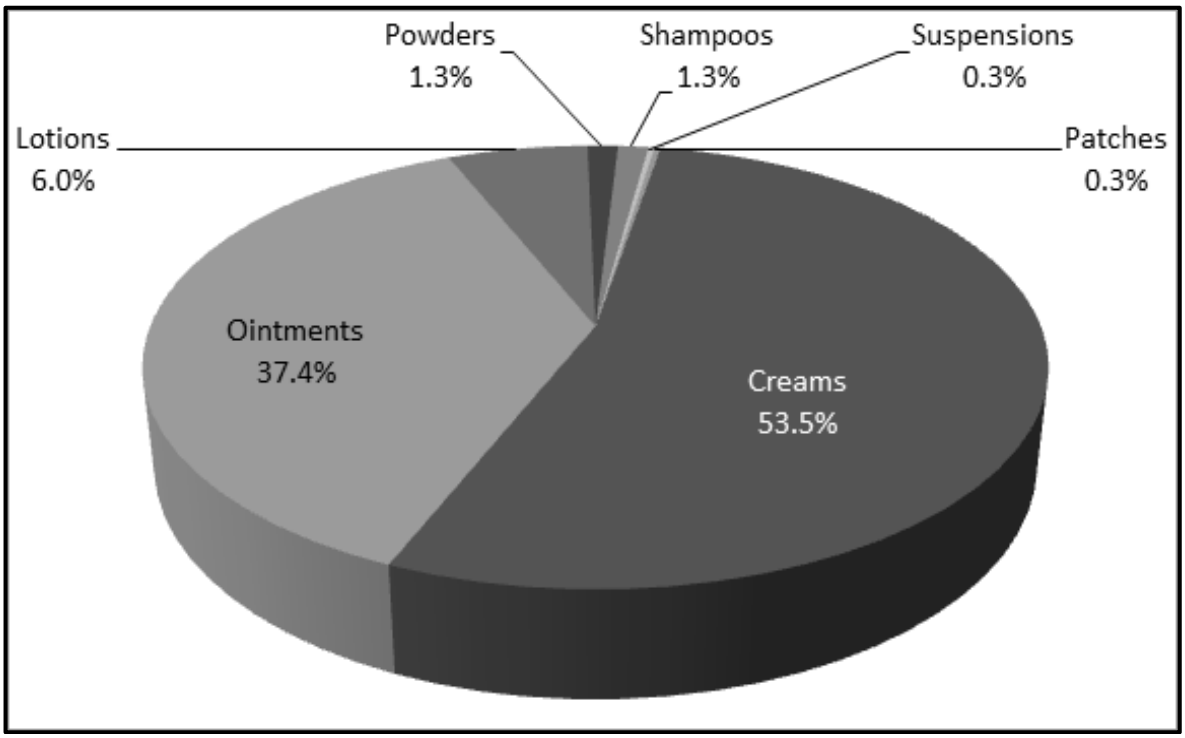

Figure 7. Types and percentages of topical dosage forms.

Figure 8 shows the registered ophthalmic dosage forms. 86.2% of the products were eye drops with the other 13.8% being eye ointments. There is a relatively small volume in the eye for topically applied products which limits the dose that can be delivered. Additionally, tear turnover and lacrimal drainage can lead to rapid clearance of applied medications. The retention time of medications can be increased by increasing the viscosity of the eye drops or by using ointments. Ophthalmic preparations are sterile and have to be used within 2 – 4 weeks of opening the product container.

The otic products listed were all liquid formulations (ear drops). 43 registered products fell into this category representing about 0.5% of all listed products (Figure 1).

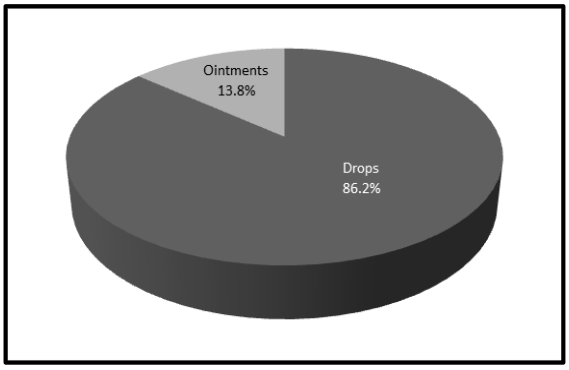

Figure 8. Types and percentages of ophthalmic dosage forms.

The type and percentage of registered products for pulmonary drug delivery are shown in Figure 9. The most common delivery devices were metered dose inhalers (76.8%) with dry powder inhalers and nebulizers accounting for 19.5% and 3.7% of the listed products. An important feature of pulmonary drug delivery is that the product container also serves as a delivery device for the drug. Metered dose inhalers (MDIs) and dry powder inhalers (DPIs) are portable unlike nebulizers. MDIs require coordination of inspiration and actuation to maximize the drug delivery to the lung. Delivery from DPIs is triggered by inhalation by the patient. However, this requires that the patient has sufficient lung function to provide a moderate to high inspiratory flow rate. There are a number of different DPI device which vary in terms of ease of use for the patient. The most common DPI devices which were observed for the registered products were the Turbuhaler^{TM} (n = 8) and the Diskus^{TM} (n = 3).

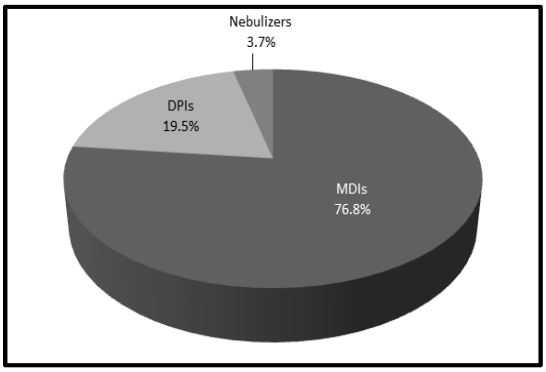

Figure 9. Types and percentages of pulmonary dosage forms. MDI – metered dose inhaler; DPI – dry powder inhaler.

Figure 10 shows the distribution of registered products for nasal administration. The products comprised of sprays, drops, and gels (61.1%, 36.1%, and 2.8%, respectively). Nasal sprays provide greater dosing accuracy, but are more expensive than drops. Nasal gels being more viscous, reduce postnasal drip and increase the retention time of the product in the nasal cavity [6].

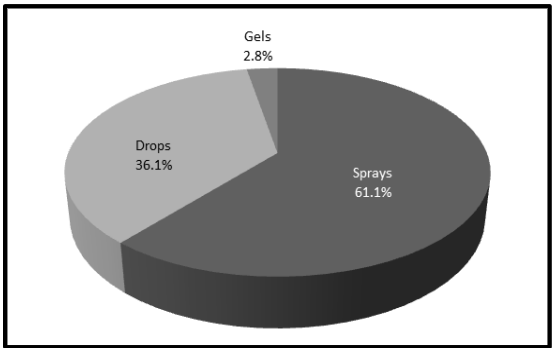

Figure 10. Types and percentages of nasal dosage forms.

Although the majority of the drugs in this category were for local delivery and therapy in the nose, there were examples in the database of registered products intended for systemic delivery (desmopressin and calcitonin). For low dose biological products with suitable permeability through the nasal mucosa, the nasal route presents an alternative route of administration to parenteral delivery via injections.

The dosage forms for rectal drug delivery that were listed comprised entirely of suppositories (97.6%) with the remaining 2.4% of the products classified as enemas (Figure 11). Drug delivery via this route may be for local or systemic effect. It is an alternative route of administration for systemic delivery of drugs for patients who may be unwilling or unable to take oral dosage forms and pediatric patients who are particularly sensitive to receiving medications via injections. Suppositories are semi-solid dosage forms that melt, dissolve or soften after administration while enemas are liquid dosage forms.

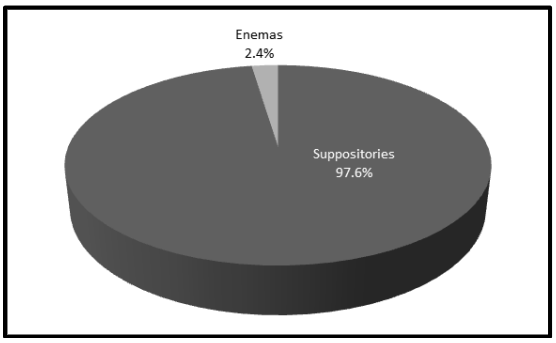

Figure 11. Types and percentages of rectal dosage forms.

The types and percentages of products for vaginal drug delivery are shown in Figure 12. There was a wide variety of dosage forms listed comprising predominantly of tablets (39.7%), pessaries (34.9%), creams (11.1%), and ovules (9.5%). Other products listed were suppositories (1.6%), gels (1.6%), and capsules (1.6%). There was overlap in some categories. For example, pessaries and vaginal suppositories are equivalent dosage forms. The term ovule is often used to refer to soft gelatin capsules used for vaginal drug delivery [7].

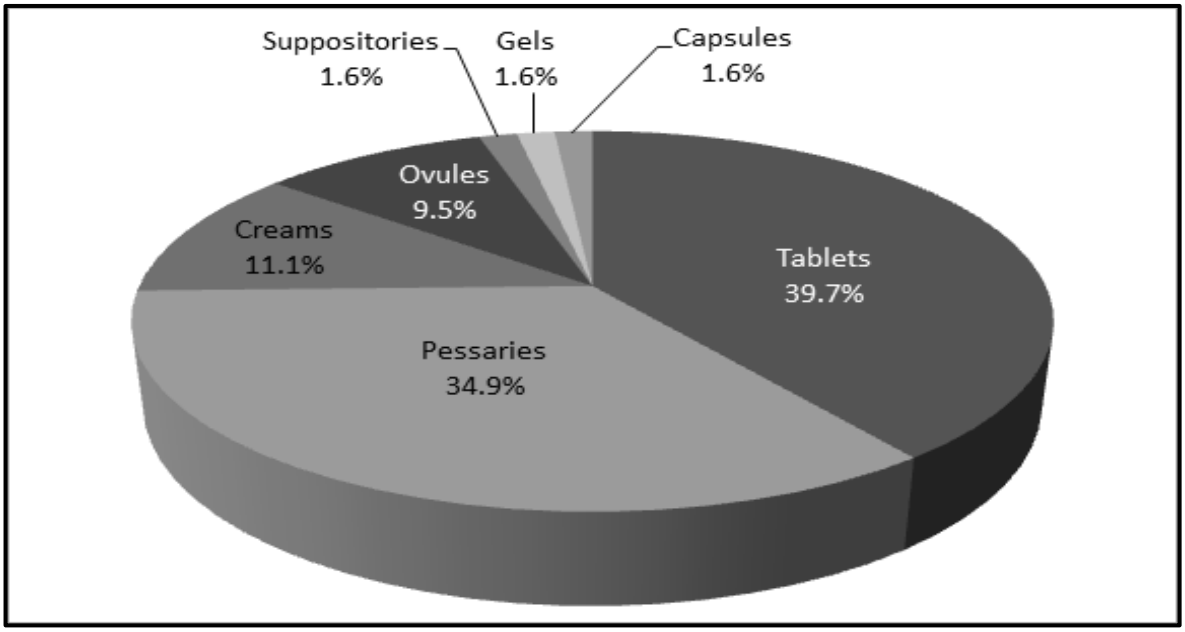

Figure 12. Types and percentages of vaginal dosage forms.

Of the ten routes of administration that were matched to products in the study, only the transdermal route featured a very small number (2) of registered products. One of the issues may be the higher cost of transdermal products compared to equivalent oral products [8]. However, this may not always be the case since studies have shown that for certain indications the cost differences between transdermal and oral products may be minimal [9]. A major benefit of transdermal delivery is a reduction in dosing frequency due to the sustained release of the drug from the transdermal patch.

The other major drug delivery route where sustained release products are often utilized is the oral route. To determine the number of registered oral sustained release products, the database was searched for these products. While the database does not specifically designate products as sustained release, search criteria using common terms or suffixes for these products can be used to identify them. Examples of common terms and suffixes used for sustained release products include: retard, CR (controlled release), ER, XL, XR (all for extended release), LA (long acting), and SR (sustained release) [10]. In most cases these terms are interchangeable and usually indicate that the drug product has been designed to release the drug over an extended period of time. A total of 110 products were identified as oral extended release products of which 87 were tablets and 23 were capsules. Each of these values account for approximately 2% of all registered oral tablets and capsules.

CONCLUSION

The study found that there is a wide variety of dosage forms and routes of administration based on an evaluation of locally registered products in Kenya. The oral, parenteral, and topical routes accounted for the majority of the products, although there were listed products from seven other routes of administration. A wide variety of specific dosage forms was observed.

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