



# **Use of Liquid Pharmaceutical Forms and Correct Handling of Solid Forms in the Dysphagic Patient**

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## **Authors' contributions**

*This work was carried out in collaboration among all authors. Author EM he had the idea of writing it, supervised the work and wrote the part relating to the manipulations of pharmaceutical forms in the "discussions" section; Author AM and the others contributed to the development of the introduction, materials and methods and part of the discussion. The conclusions were written and reviewed by all the authors together. All authors read and approved the final manuscript.*

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## **ABSTRACT**

**Introduction:** The presence of dysphagia is a rather common event, both physiologically in elderly people and the presence of neurological, maxillofacial, or upper digestive pathologies. Many drugs are routinely taken in solid form for the convenience of use, however, in such patients, it becomes difficult to swallow tablets or capsules and it is important to both have liquid alternatives and possibly handle the solid forms correctly. In this article, we want to describe the correct handling of solid pharmaceutical forms or the transition to liquid ones where present.

**Methodology:** the article was written by integrating one's knowledge of pharmacology and pharmaceutical techniques with printed material and online articles extracted from databases google scholar and PubMed.

**Discussion and Conclusions:** The liquid forms, where they exist, are important in the management of drug therapy in the dysphagia patient. In the absence of therapeutic alternatives or liquid forms of the same principle, the solid forms can be manipulated within certain limits, paying

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attention to the interactions with nutritional mixtures and other drugs and above all not obstructing the probe and not compromising the kinetic and dynamic characteristics of the active ingredient.

*Keywords: Dysphagia; pharmaceutical forms; drug handling; clinical galenic.*

## 1. INTRODUCTION

Dysphagia is a very common symptom, especially in the elderly and in patients with neurological problems, and is defined as difficulty in the formation and transit of the food bolus in the upper digestive tracts. It is so common in the elderly that it is often framed as a true geriatric syndrome [1]. The distinction between oropharyngeal and esophageal refers to the main lesion site; Oropharyngeal dysphagia is the difficulty in getting material from the oropharynx to the esophagus, caused by a functional abnormality upstream of the esophagus. Patients complain of difficulty initiating swallowing, nasal regurgitation, and tracheal aspiration followed by a cough. Generally, it's the most frequent, with a prevalence in the general population of about 16% but increases with age up to 30% in the elderly up to 40-60% in the institutionalized [2]. In particular, oropharyngeal dysphagia affects up to 80% of patients with neurodegenerative diseases and stroke outcomes. It represents the cause of mortality and morbidity due to ab ingests phenomena and the risk of malnutrition and dehydration. The swallowing system includes the pharynx, the upper esophageal sphincter (cricopharyngeal), the body of the esophagus, and the lower esophageal sphincter. The upper third of the esophagus and the structures proximal to it are made up of striated muscle; the distal esophagus and the lower esophageal sphincter are made up of smooth muscle. These components work as an integrated system that carries the material from the mouth to the stomach and prevents its reflux into the esophagus. Physical obstruction or disorders that interfere with motor function (esophageal motility disorders) can affect the system [3]. The presence of dysphagia is also a factor that complicates adherence to drug therapies: because most of the drugs used in chronic therapies are given by mouth, dysphagia implies difficulty in adherence and possible complications related not only to ab ingests phenomena but also to the underdose caused by the failure to take the prescribed doses and to the difficulty of the patient and the caregiver in long-term management [4]. These patients are often placed in enteral feeding with probes (PEG

or nasogastric tube) and this further complicates the administration of oral drugs. Handling the oral solid pharmaceutical form of drugs is a widely used practice frequently by health professionals, patients, and family members, and caregivers to encourage adherence to oral therapy in patients with swallowing difficulties [5]. The handling requires that the drug is pulverized, mixed with water, or included in fruit puree and subsequently administered to the patient. In this article we want to describe the correct methods of managing these therapies, with particular attention to the administration of solid pharmaceutical forms after their handling and what is the role of liquid formulations in their replacement [6].

## 2. METHODOLOGY

The article aims to be a mini-review integrating some literature data with the individual knowledge of the authors of pharmacology and pharmaceutical technique (in addition to their practical experience). The online articles used were extracted from Google Scholar and PubMed databases, as well as a book of pharmaceutical techniques and printed material. They were selected from among those relating only to the biopharmaceutical aspects of the formulations and the related manipulations of pharmaceutical forms for oral use, using articles published from 1990 to today.

## 3. RESULTS AND DISCUSSION

Today, the preferred mode of administration of drugs is the oral one. Solid oral pharmaceutical forms (SODFs) include tablets, capsules, and granules. The advantages are the simplicity of the preparation methods and packaging, product stability, ease of administration and dosing accuracy and greater microbiological stability [7]. One of the factors that influence the functionality of the drug is the good choice of excipients, according to which SODFs is classified as conventional and modified release. In the first case, the dissolution of the drug depends on its intrinsic properties of solubility. In the second case, on the other hand, the type of formulation modulates the release of the active ingredient

and therefore the relative trend of the blood levels. SODFs must be swallowed intact, because only through the correct intake can they meet disintegration, dissolution, and release of the contents into the lumen gastrointestinal [8]. Despite the administration of these pharmaceutical forms being advantageous because it is simple and non-invasive, it starts from the assumption that swallowing is a stable function time. Inappropriate handling of the drug is a common practice to remedy the problem both in general populations and in health care settings. Manipulations consist of splitting or crushing the tablets and opening out the capsules to mix them with food or dissolve them in water [9]. These practices lead to the loss of efficacy of the drug because they modify its absorption, stability, and effect. They also increase the likelihood of administering an incorrect or insufficient dosage and, in the case of dragees or film-coated forms, the result can be an unpleasant tasting preparation. It should also be noted that for drugs with a low therapeutic index (for example antiepileptics, digoxin, anticoagulants, antibiotics, etc.) there may be the risk of exposure of the operator to toxic doses of the substance and also of iatrogenic damage from overexposure of the patient to toxic quantities of the substance [10]. An initial assessment should be made if alternative pharmaceutical forms of the same drug exist on the market, now available for most of the more commonly used products. The distinction between:

- LAF (long-acting formulations), such as example transdermal patches, subcutaneous implants, depot preparations, or pharmaceutical forms with modified release, gastroprotective or delayed-release, which release the active ingredient very slowly into the circulation, reaching lower maximum doses and in a long time but kept longer [11]
- SAF (short-acting formulations), all those with an immediate release such as sublingual, buccal, effervescent tablets, liquid formulations (oral drops), transmucosal, etc ... which give rapid absorption peaks and in higher concentrations [12].

When a drug should be administered orally to a patient with swallowing difficulties, during the prescription phase, it must be previously evaluated, whether it's possible, to avoid manipulation and therefore if there is an

alternative route of administration of the drug (e.g. transdermal, injection) which, at the same of clinical indications and efficacy, doesn't require manipulations or if there is an alternative oral pharmaceutical form of the drug that requires less handling (oral drops, syrup, effervescent tablet, gold-dispersible tablet, granules for oral suspension, etc.) or if there is another drug (in therapeutic equivalence) that doesn't require manipulation [13]. If the patient is being treated with a prolonged-release formulation, for example, tablets, switching to a transdermal patch or liquid formulation (for example syrup) of an equivalent compound with a long half-life may be valid alternatives, as well as switching from a solid to a liquid formulation both with the rapid release [14]. The liquid formulations have interesting advantages, first of all, the possibility of administration with a probe, in general after dilution, without obstructing the probe or adhering excessively to its walls causing underdosing. On the other hand, the direct manipulation of solid formulations in the absence of therapeutic alternatives is more complex. This provides for crushing and pulverizing tablets or granules and opening of the hard capsules with the withdrawal of the solid content, both followed by liquid dilution of the obtained compounds and subsequent administration [15]. Attention must always be paid to the package leaflet (product characteristics) as it is always reported, among the methods of administration, the possible possibility of dividing/crushing tablets or opening the capsules. It should also be noted that different pharmaceutical forms of the same drug may have different indications; for example, trazodone exists in both scored and extended-release, non-divisible tablets [16]. To avoid errors in administration, always read the single package leaflet first. In summary, the manipulation of tablets (trituration) and capsules (opening) can only be carried out when it is guaranteed that:

- the patient is given the full dose of medication prescribed (there should be no loss of drug during handling)
- the manipulated drug maintains its stability until it is taken
- the manipulated drug is absorbed in the desired rate, to ensure the therapeutic effect
- there is no toxicity caused by the manipulation either for the patient or for the healthcare worker
- there is no interaction with food and drink so that both the drug and the nutrient come absorbed effectively and the site of

administration is still the site of absorption of the drug

- the manipulated drug does not obstruct the gastrointestinal probe and/or does not cause gastrointestinal symptoms resulting from incorrect administration in the probe [17,18,19].

In the first place there are pharmaceutical forms that cannot be manipulated due to biopharmaceutical problems of the active ingredient; these are soft capsules (there is no accurate and complete withdrawal of the dose), coated tablets (they do not maintain stability due to exposure to air, humidity, light or become irritating to the mucous membranes or take on unpleasant organoleptic characteristics), tablets/capsules and micro granules with a gastro-resistant coating (acid-labile drugs are exposed to gastric acidity and are inactivated by it, consequently losing their effectiveness) and modified-release forms (the drug is not released gradually to maintain a constant plasma concentration and evoke a maintained therapeutic effect over time, but everything is released immediately, with an initial risk of overexposure and toxicity, followed by underexposure and lack of efficacy) [20]. Moreover, in case you decide to carry out the manipulation, specific tools such as pill cutters or pill crushers must be used, available in pharmacies at low prices and which allow greater accuracy in the procedure.

### 3.1 Specific Indications for Some Pharmaceutical Forms

For oral administration, if the drug can be manipulated:

- crush the tablet, dissolve in a little water or mix in apple puree and administer immediately
- open the capsule, dissolve in a little water or mix in apple puree and administer immediately

In case of administration by the gastrointestinal tube; If the drug can be manipulated:

- do not use syringes with a volume of fewer than 20 ml (to avoid excessive pressure exerted on the probe) [21]
- stop feeding and wash the tube with 30 ml of water
- don't mix the drug with the nutritional product: the drug potentially interacts with

the nourishing and alters the chemical-physical characteristics of the nutritional product

- prepare the drug immediately before administration
- prepare and administer one drug at a time
- wash the tube with 30 ml of water between one drug and another and at the end of the administration of the medications, before eventually resuming nutrition
- respect the time of administration of the nutrient concerning the drug.

For drugs that must be taken on an empty stomach, suspend the nutritional product one hour before and resume it 1-2 hours later; for drugs that must be taken on a full stomach: administer the nutritional product in time near the drug. Don't administer PEG drugs in sublingual tablets (not adequate absorption of the drug and not immediate effect of the drug).

It should be considered also the possibility, as an alternative to the direct manipulation from the patient or the caregiver of the SODFs, to contacting a galenic pharmacy for the production of alternative pharmaceutical forms, sometimes not even available as industrial products. This involves the lowest risk of damage related to the possible sometimes incorrect handling of the drug by the patient and, above all, to the guarantee of a professional intervention performed in a galenic laboratory, with high standards and quality assurance of the finished product. Finally, in the case of patients with prevalent dysphagia for liquids, it is possible to use liquid preparations with the addition of thickeners or directly gelled water as a vehicle to allow oral intake, with an attention to the fact that the rheological modification of the liquid can, in any case, modify the properties of the release of the active ingredient, especially for gastric emptying and possible disintegration or dissolution from the gel mesh and passage into solution in intestinal fluids [22].

## 4. CONCLUSIONS

The liquid forms, where they exist, are very important in the management of drug therapy in the dysphagia patient [23]. In the absence of therapeutic alternatives or liquid forms of the same active ingredients, the solid forms can be manipulated within some limits, with big attention to the interactions with nutritional mixtures and other drugs and above all not to obstruct the probe and not to compromise the kinetic and

dynamic characteristics of the active ingredient [24]. Clinical galenic allows for obtaining customized forms of solutions, suspensions, emulsions, or syrups and also mixing some active ingredients in gelled water or by formulating solutions and then using thickeners for patients with dysphagia for liquids [25]. However, it must be said that these procedures must be performed only if you are sure of the stability of the active principle in the various excipients/vehicles and paying attention to interactions with other drugs or nutritional mixtures and not to compromise the kinetic and dynamic properties of the drugs [26].

## CONSENT AND ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

- Ershov VI, Zdvizhkova SV, Gonchar-Zaikin AP, Lozinskaya TY, Kuznetsov GE, Borodkin IN, Silkin VV. Éffektivnost' lecheniia narushennoi funktsii glotaniia u patsientov s ishemicheskim insul'tom i neirogennoi disfagiei v ramkakh otdeleniia reanimatsii i intensivnoi terapii [The treatment efficacy of disturbed swallowing function in patients with ischemic stroke and neurogenous dysphagia in the intensive care unit]. Zh Nevrol Psikhiatr Im S S Korsakova. 2019;119(7):35-40. Russian. DOI: 10.17116/jnevro201911907135. PMID: 31464287.
- Aaltonen LM, Saarela M, Jousimaa J, Aherto A, Arkkila P. Dysphagia--moniammatillinen haaste [Dysphagia--a multidisciplinary challenge]. Duodecim. 2009;125(14):1535-44. Finnish. PMID: 19711576.
- Cho YK. [Pharmacological Treatments of Esophageal Dysphagia]. Korean J Gastroenterol. 2021 Feb 25;77(2):71-76. Korean. doi: 10.4166/kjg.2021.024. PMID: 33632997.
- Eichenwald EC; Committee on Fetus and Newborn. Diagnosis and Management of Gastroesophageal Reflux in Preterm Infants. Pediatrics. 2018;142(1):e20181061. DOI: 10.1542/peds.2018-1061. Epub 2018 Jun 18. PMID: 29915158
- Sura L, Madhavan A, Carnaby G, Crary MA. Dysphagia in the elderly: management and nutritional considerations. Clin Interv Aging. 2012;7:287-98. DOI: 10.2147/CIA.S23404. Epub 2012 Jul 30. PMID: 22956864; PMCID: PMC3426263.
- Shigematsu T, Fujishima I. [Dysphagia and swallowing rehabilitation]. Brain Nerve. 2015 Feb;67(2):169-82. Japanese. DOI: 10.11477/mf.1416200109. PMID: 25681362.
- Lawlor CM, Choi S. Diagnosis and Management of Pediatric Dysphagia: A Review. JAMA Otolaryngol Head Neck Surg. 2020;146(2):183-191. DOI: 10.1001/jamaoto.2019.3622. PMID: 31774493.
- Johnston BT. Oesophageal dysphagia: a stepwise approach to diagnosis and management. Lancet Gastroenterol Hepatol. 2017 Aug;2(8):604-609. DOI: 10.1016/S2468-1253(17)30001-8. PMID: 28691686.
- Duffy KL. Dysphagia in Children. Curr Probl Pediatr Adolesc Health Care. 2018 Mar;48(3):71-73. DOI: 10.1016/j.cppeds.2018.01.003. PMID: 29571543.
- Aoyagi Y, Inamoto Y, Shibata S, Kagaya H, Otaka Y, Saitoh E. Clinical Manifestation, Evaluation, and Rehabilitative Strategy of Dysphagia Associated With COVID-19. Am J Phys Med Rehabil. 2021 May 1;100(5):424-431. DOI: 10.1097/PHM.0000000000001735. PMID: 33657028; PMCID: PMC8032217.
- Jadcherla S. Dysphagia in the high-risk infant: potential factors and mechanisms. Am J Clin Nutr. 2016 Feb;103(2):622S-8S. doi: 10.3945/ajcn.115.110106. Epub 2016 Jan 20. PMID: 26791178; PMCID: PMC4733255.
- Bielefeldt K, Berges W. Therapie der funktionellen Dysphagie [Therapy of functional dysphagia]. Dtsch Med Wochenschr. German. 1989;114(39):1492-5. DOI: 10.1055/s-2007-1024467. PMID: 2676449.
- Brodsky MB, Mayfield EB, Gross RD. Clinical Decision Making in the ICU: Dysphagia Screening, Assessment, and Treatment. Semin Speech Lang. 2019; 40(3):170-187.

- DOI: 10.1055/s-0039-1688980. Epub 2019 Jun 3. PMID: 31158902.
13. Philipsen BB, Mortensen HR, Melgaard D. [Dysphagia]. *Ugeskr Laeger*. 2019;181(9):V09180594. Danish. PMID: 30799809.
14. Wirth R, Dziewas R. Neurogene Dysphagie [Neurogenic dysphagia]. *Internist (Berl)*. 2017;58(2):132-140. German. DOI: 10.1007/s00108-016-0178-8. PMID: 28084502.
15. Miller S, Diers D, Jungheim M, Schnittger C, Stürenburg HJ, Ptok M. Studying effects of neuromuscular electrostimulation therapy in patients with dysphagia: which pitfalls may occur? A translational phase I study. *Ger Med Sci*. 2021;19:Doc07. DOI: 10.3205/000294. PMID: 34194290; PMCID: PMC8204381.
16. Guillen-Sola A, Soler NB, Marco E, Pera-Cegarra O, Foro P. Effects of prophylactic swallowing exercises on dysphagia and quality of life in patients with head and neck cancer receiving (chemo) radiotherapy: the Redyor study, a protocol for a randomized clinical trial. *Trials*. 2019 Aug 14;20(1):503. DOI: 10.1186/s13063-019-3587-x. PMID: 31412947; PMCID: PMC6694466.
17. Wang Z, Song WQ, Wang L. Application of noninvasive brain stimulation for post-stroke dysphagia rehabilitation. *Kaohsiung J Med Sci*. 2017;33(2):55-61. DOI: 10.1016/j.kjms.2016.11.007. Epub 2016 Dec 27. PMID: 28137412.
18. Dylczyk-Sommer A. Dysphagia. Part 1: General issues. *Anaesthesiol Intensive Ther*. 2020;52(3):226-232. DOI: 10.5114/ait.2020.98074. PMID: 32876410.
19. Bruckstein AH. Dysphagia. *Am Fam Physician*. 1989;39(1):147-56. PMID: 2643274.
20. Stegemann S, Gosch M, Breitzkreutz J. Swallowing dysfunction and dysphagia is an unrecognized challenge for oral drug therapy. *Int J Pharm*. 2012;430(1-2):197-206. DOI: 10.1016/j.ijpharm.2012.04.022. Epub 2012 Apr 15. PMID: 22525080.
21. Kruger D. Assessing esophageal dysphagia. *JAAPA*. 2014 May;27(5):23-30. DOI: 10.1097/01.JAA.0000446227.85554.fb. PMID: 24691181.
22. Payne MA, Morley JE. Dysphagia: A New Geriatric Syndrome. *J Am Med Dir Assoc*. 2017 Jul 1;18(7):555-557. DOI: 10.1016/j.jamda.2017.03.017. Epub 2017 May 16. PMID: 28526586.
23. Fashner J, Gitu AC. Common gastrointestinal symptoms: dysphagia. *FP Essent*. 2013 Oct;413:11-5. PMID: 24124702.
24. Dylczyk-Sommer A. Dysphagia. Part 2: Dysphagia in intensive care patients. *Anaesthesiol Intensive Ther*. 2020;52(3):233-236. DOI: 10.5114/ait.2020.98490. PMID: 32876411.
25. Paterson WG. Dysphagia in the elderly. *Can Fam Physician*. 1996;42:925-32. PMID: 8688695; PMCID: PMC2146388.

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