H2020-MSCA-ITN-2020 (ETN)

AGePOP

Project No. 956146

Drug **A**bsorption in **Ge**riatric **P**atients and **O**lder **P**eople:
a training network innovating drug development for the advanced age population

Deliverable D4.5

White Paper

WP 4 – Outreach – Public engagement, dissemination and exploitation

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Delivery date	30/12/2024
Dissemination level	Public
Type	Report

Version 1.0

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 956146.

Revision History

Author(s)	Description	Date
Susanne Page (ROCHE), Cordula Stillhart (ROCHE)	Draft deliverable	13/11/2024
Werner Weitschies (UG), Christos Reppas (NKUA)	Revision 1	04/12/2024
Maria Vertzoni (NKUA)	Revision 2	23/12/2024
Jacqueline Strehler (accelCH)	Revision 3	27/12/2024
Maria Vertzoni (NKUA)	Final version	27/12/2024

Contents

Abbreviations

EC	European Commission
EU	European Union
H2020	Horizon 2020
WP	Work Package

Partner Short Names

Abbvie	AbbVie Deutschland GmbH & Co KG
accelCH	accelopment Schweiz AG
AZ	AstraZeneca AB
Bayer	Bayer AG
Janssen	Janssen Pharmaceutica NV
KUL	Katholieke Universiteit Leuven
Merck	Merck Healthcare KGAA
NKUA	National and Kapodistrian University of Athens
Novartis	Novartis Pharma AG
Red Cross Hospital	Korgialenio-Benakio Red Cross Hospital
Roche	F. Hoffmann- La Roche AG
UCB	UCB Pharma GmbH
UG	Universität Greifswald

Executive summary

Background	Objectives
AGePOP White Papers will provide guidance on drug formulation for older adults and geriatric patients. It is a unique opportunity to disseminate AGePOP research results to key audiences.	The 1st AGePOP White Paper is intended to disseminate the first part of ESRs' findings and make these results accessible through the AGePOP website in order to reach the general public but also researchers and key stakeholders.
Impact	**Next steps**
As the primary online platform for the project, the AGePOP website serves as a crucial hub for sharing information, engaging stakeholders, and ensuring that the AGePOP's objectives, progress, and outcomes are effectively communicated to a broader audience. By publishing the White Papers online, the project seeks to reach a diverse audience, including the general public and key stakeholders, fostering greater understanding and collaboration.	AGePOP intends to publish a White Paper in an open-access journal, offering guidance on drug formulation tailored to older adults and geriatric patients. By highlighting best practices, identifying knowledge gaps, and offering guidance on drug formulation for older adults and geriatric patients, this publication aims to foster early interest and active engagement from key stakeholders in the drug approval process.

Legal disclaimer: The AGePOP project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 956146. The sole responsibility for the content of this publication lies with the authors. It does not necessarily reflect the opinion of the European Commission (EC).

1 White paper

As time swiftly passes, our AGePOP project is nearing its conclusion. Now is the perfect moment to reflect on the valuable insights we've gained over the past four years.

We had the support of almost 800 older adults and more than 300 young healthy volunteers across the different studies within the AGePOP project. We extend our heartfelt gratitude to all participants! Their contributions have enabled us to deepen our understanding of gastrointestinal physiology and gather significant knowledge about pharmacotherapy in older adults and geriatric patients. Their participation has greatly contributed to the advancement of science for the benefit of society.

Despite this encouraging fact, there are also several challenges that geriatric patients face when participating in clinical studies. One factor that significantly hinders the participation of older adults and geriatric patients in clinical studies is the high prevalence of polypharmacy within this age group. The complexities associated with taking multiple medications often lead to the exclusion of these patients from clinical studies, as co-medications may confound the study results. Our research clearly demonstrated that the prevalence of polypharmacy - defined as the intake of five or more medications - varies depending on the setting. Results from two different studies in Germany showed that the prevalence in a hospital is around 96%% [1, 2], while it was 59% in the home settings [2]. This also indicates that multimorbid patients often require more medical support compared to their healthier counterparts.

With respect to oral dosage forms, older adults prefer solid forms (e.g., tablets) over liquid forms (e.g., syrups) [2] and find tablets easier to swallow than capsules [3]. Research comparing the swallowability, visual perception, and handling of tablets demonstrated that both young and older adults can swallow a wide variety of tablets of different sizes and shapes, although they tend to underestimate their own swallowing abilities [3]. The primary factor affecting the subjective rating of swallowability is the tablet's size, followed by its shape and surface characteristics. The significance of surface characteristics was highlighted in a study examining the effects of different surfaces on esophageal transit, a crucial factor for the safe and efficient administration of solid oral dosage forms. The study demonstrated a clear advantage of film-coated tablets over uncoated tablets and hard gelatin capsules in facilitating esophageal transit [4]. Overall, we observed that swallowability significantly impacts the willingness to take tablets regularly, especially over longer time periods [1].

In addition to evaluating the acceptability of solid oral dosage forms, we conducted questionnaire-based studies to explore the real-life dosing conditions in this patient population. Generally, older adults typically take their medications immediately after a meal and tend to take all their medications together (49%) rather than separately (28%) [2, 5]. The volume of liquid typically used to swallow the medication is quite variable (see Figure 1). The majority of older adults take their medicine with a small glass (100 mL, 32%), a few sips (50 mL, 28%), and a larger glass (200 mL, 25%) of liquid. While the majority of individuals use tap or mineral water (55%), some also use sparkling water (32%), tea (19%), or other drinks for taking their medicine (details are presented in Figure 2) [2, 5]. Additional studies have demonstrated that the use of sparkling water and black tea could influence the pharmacokinetics of drugs in certain cases [6, 7].

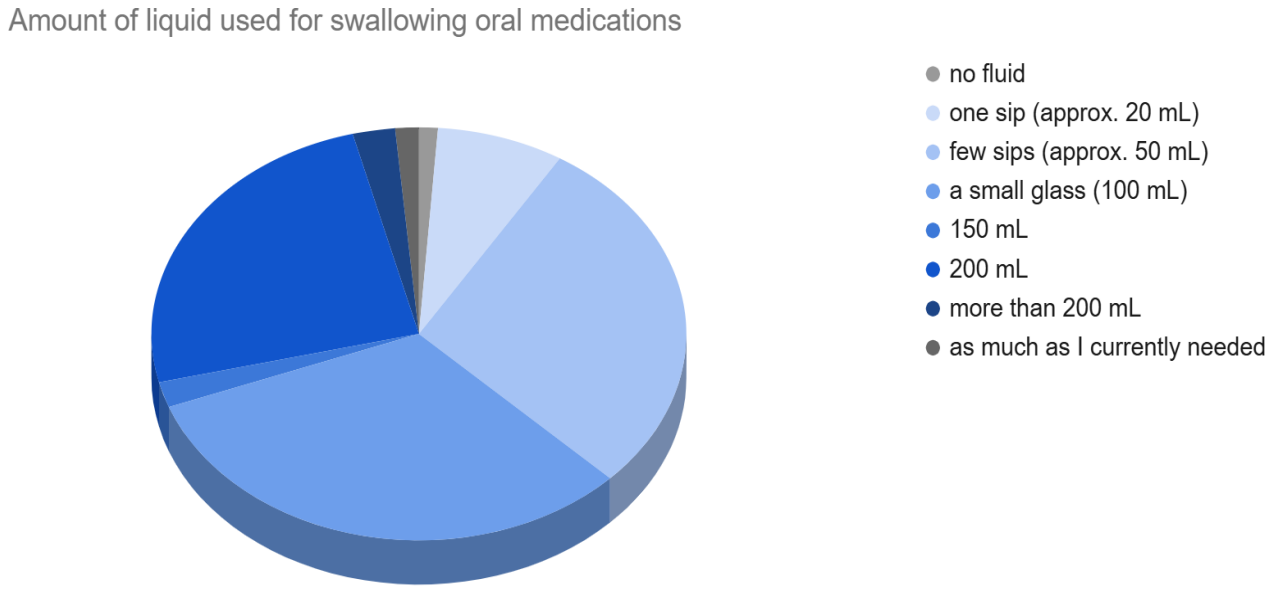

Figure 1. Amount of liquid used for swallowing oral medications [2, 5].

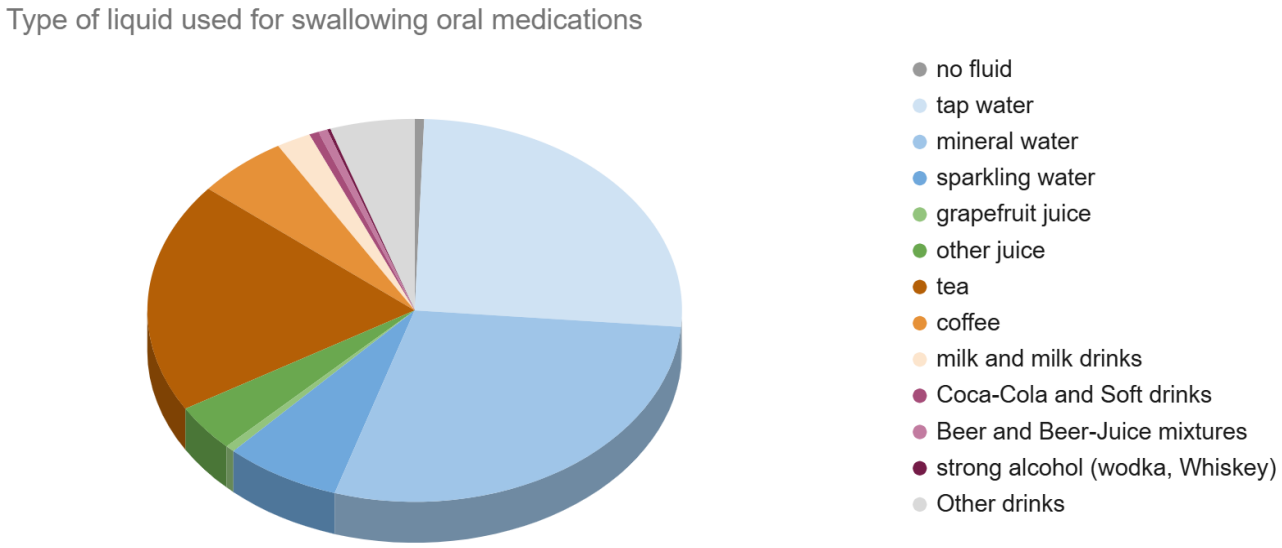

Figure 2. Type of liquid used swallowing oral medications [2, 5].

One of the primary focuses of the AGePOP Consortium has been the investigation of gastrointestinal physiology in older adults and geriatric patients. It is well-known that the digestive system matures during early childhood, and certain diseases and treatments can modify the characteristics of the stomach and intestines. Such changes can directly influence how drugs are absorbed when taken orally. Therefore, it is crucial to understand how the gastrointestinal tract changes in older and geriatric patients and how ageing affects drug absorption.

In our studies, we measured the volumes and pH levels of gastric and intestinal fluids, as well as the time required for the stomach contents to empty into the intestine, in older adults before and after meal intake. Overall, our data indicated that aging alone does not alter these properties. However, we observed a significant increase in stomach pH among older adults, which is attributed to the frequent use of medications designed to reduce stomach acidity [8]. This finding highlights the importance of considering the complex clinical conditions, including the multiple medications often taken concurrently by older and geriatric populations.

In general, polypharmacy/multimorbidity makes the investigation of the impact of chronological aging on gastrointestinal physiology and oral drug absorption difficult. However, other studies have demonstrated that reduced function of other organs, such as the kidneys, and other age-related factors can lead to differences in pharmacokinetics between younger and older patients [9, 10]. This is a crucial consideration in pharmacotherapy and the clinical development of new medications. The pharmacokinetics of drugs in geriatric patients may significantly differ from those observed in a typical clinical study population [10], underscoring the importance of including these populations in clinical trials.

Ultimately, a deeper understanding of the complexities involved in drug pharmacokinetics in geriatric patients will facilitate the development of advanced in vitro and in silico modeling tools. These tools will better predict the overall impact of aging and disease conditions on drug absorption, distribution, metabolism, and elimination in older individuals and geriatric patients. Such advancements are essential for enhancing the safety and efficacy of medications and reducing the need for clinical trials in this vulnerable population.

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