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The Development of the Oral Controlled Absorption System (OCAS®): A New Improved Formulation of Tamsulosin

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1. Introduction

Lower urinary tract symptoms suggestive of benign prostatic hyperplasia (LUTS/BPH) is the most common urological condition in older men. Approximately 25% of men aged 40 years and over report LUTS [1,2]. As the prevalence of LUTS increases with age and the population in most European countries is ageing, the number of older men which will present with LUTS/BPH will dramatically increase in the next 2 decades [3]. Although voiding symptoms are more prevalent in patients with LUTS/BPH, storage symptoms and in particular nocturia are considered as the most bothersome symptoms [4].

Since the introduction of several pharmacological therapies in the 1990s, there has been a decrease in the number of transurethral resections of the prostate (TURPs) with a parallel increase in the number of prescriptions [3]. In the Triumph (TransEuropean Research Into the Use of Management policies for LUTS/BPH in Primary Healthcare), 75% of over 10,000 European LUTS/BPH patients received a pharmacological therapy as initial treatment [5].

Today, α_1-adrenoceptor (AR) antagonists are the mainstay treatment for most patients with bothersome LUTS/BPH. For patients at risk of progression to acute urinary retention (AUR) or invasive therapy such as those with a large prostate or high prostate specific antigen (PSA), an α_1-AR antagonist in combination with a 5α-reductase inhibitor is the most appropriate treatment [6]. Of the currently available α_1-AR antagonists, the conventional tamsulosin 0.4 mg capsule has the most favourable efficacy/tolerability ratio [7] and is the most frequently prescribed pharmacological therapy in Europe [5]. This is probably related to its relative selectivity for α_{1A} and α_{1D}-AR subtypes in the LUT as compared to α_{1B}-AR subtypes in the blood vessels of

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particularly older people and its enrichment in LUT tissues [8].

2. OCAS®: oral controlled absorption system

One of the drawbacks of the existing conventional tamsulosin formulation is the fact that the exposure to tamsulosin [9] and the risk of orthostatic hypotension [10] increases if it is taken without food/on an empty stomach [8]. In addition, drug release from controlled release systems such as the conventional tamsulosin formulation is dependent on the presence of water in the gastro-intestinal (GI) tract [11]. As water is poorly available in the colon, the release (and therefore absorption) of drug from controlled release formulations such as the conventional tamsulosin formulation is impeded in this part of the GI tract (Fig. 1) [8].

Therefore, Yamanouchi has developed a new controlled release delivery system, the oral controlled absorption system (OCAS®), in order to ensure continuous and consistent drug release throughout the entire GI tract and to achieve consistent 24-hour plasma concentrations (Fig. 2) [8,11,12]. OCAS tablets are of a gel matrix type which contains a gel-enhancing agent polyethylene glycol which ensures very rapid and nearly complete gelation/hydration of a hydrophilic gel-forming polyethylene oxide in the upper part of the GI tract (stomach and small intestine) [11]. The gel matrix is then maintained in the hydrated state in the colon and therefore has sufficient strength to maintain drug release in the colon although water is poorly available there (Fig. 1) [8,12]. OCAS technology is also pH-independent and drug release from this formulation is relatively free of food effects.

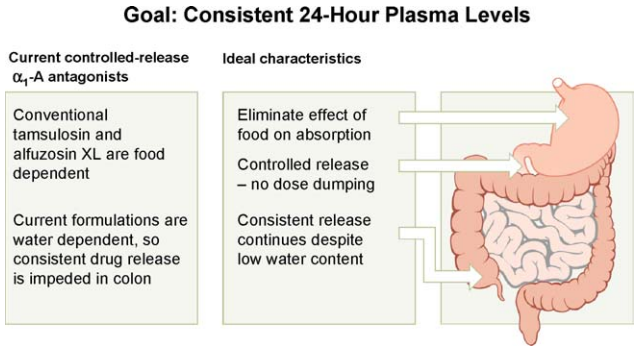

Fig. 2. Development goals for an ideal drug delivery system.

3. Pharmacokinetics of Omnic OCAS

Yamanouchi has used the OCAS technology to develop a new formulation of tamsulosin called Omnic

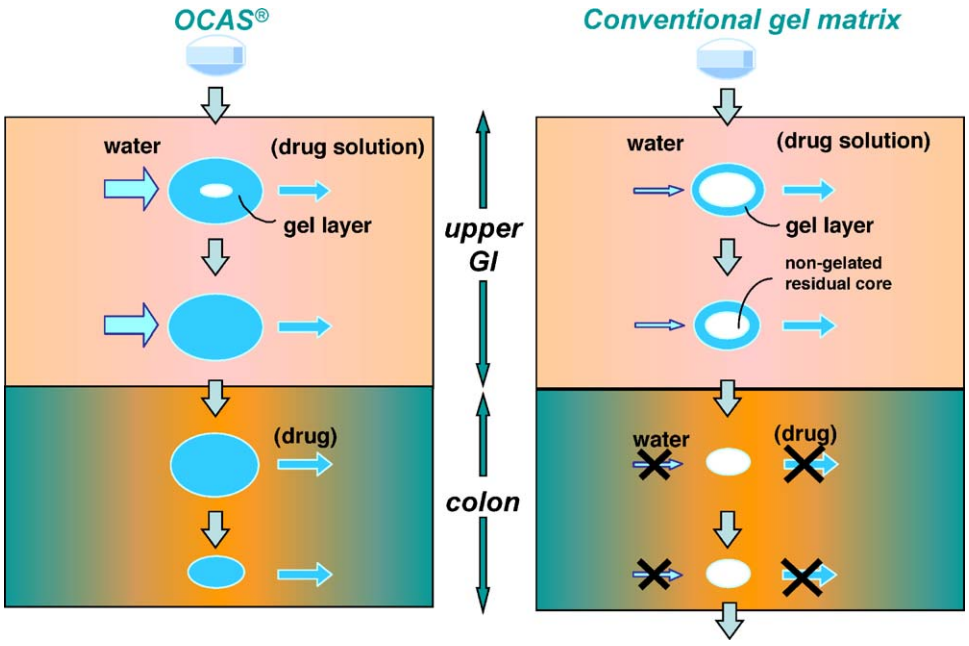

Fig. 1. Very rapid gelling and nearly complete hydration of OCAS delivery system in the upper GI tract ensures drug release throughout the entire GI tract, including the colon where water is poorly available. Reprinted from European Urology Supplements, 4(2), Michel MC, Korstanje C, Krauwinkel W, Kuipers M, The pharmacokinetic profile of tamsulosin oral controlled absorption system (OCAS®), pp 15–24, 2005, with permission from European Association of Urology [8].