Introduction
Weight loss is in theory very simple: one needs to use up more calories than one consumes. It is documented that to lose one pound (0.45 kilogram) of body weight there needs to be a negative balance of 3,500 kilocalories (kcal). However, in reality cutting down excess calories or increasing calorie expenditure via exercise might prove to be very difficult. Most community pharmacists can confirm this by the number of clients asking for recommendations on weight loss preparations. As most of the over-the-counter (OTC) weight loss preparations available on the market in Malta are classified as food supplements reliable data is lacking. In this paper the author has consulted systematic reviews and meta-analysis of randomised clinical trials of a few common ingredients in weight loss preparations available in Malta.

Citrus Aurantium
Citrus aurantium or bitter orange has been studied for weight loss as its primary constituent is p-synephrine. P-synephrine which is similar in structure to ephedrine is thought to increase basal metabolic rate and lipolysis as well as acting as a mild appetite suppressant. Unfortunately, most of the data on p-synephrine is clouded by the lack of reproducibility and poorly standardized extracts used. In a review of 23 rigorous studies published in the International Journal of Medical Science it was established that bitter orange extract and p-synephrine increase metabolism and energy expenditure and may contribute to modest weight loss if taken for up to 12 weeks in combination with dietary and exercise regimens. The loss in body weight ranged from 1.04 to 4.63 kg in the study period but the data was for preparations where citrus aurantium was only one of the ingredients. Side-effects commonly associated with ephedrine such as high blood pressure and palpitations are not to be expected with p-synephrine as it has receptor binding specificities. Again, more rigorous studies are required to determine dose and duration to be recommended for significant weight loss.

Conjugated Linoleic Acid
Conjugated linoleic acid (CLA) is a collection of isomers of linoleic acid, a polyunsaturated omega 6 fatty acid which is commonly found in dietary sources such as egg yolk, animal

Abstract
Obesity has been described as a pandemic as it is estimated to contribute to more than 3 million deaths worldwide. In Malta 28.7% of the population is obese and another 67.6% is classified as overweight. This paper will be provide a summary of systematic reviews and meta-analysis of some common ingredients in weight loss preparations available in local pharmacies.
fats and a number of oils such as peanut oil and olive oil. Animal studies have suggested that CLA has an effect on body composition and in most species it was found to reduce body fat. This data fuelled research into human studies in the hope that results would be reproducible. In a meta-analysis published in 2007 which included 20 human studies, the authors concluded that CLA causes a limited reduction in fat of about 0.09 kg weekly, around 1 kg every 3 months. This loss was not reproducible in all studies because efficacy is highly dependent on factors such as type of isomer used, dose and duration. It has been recommended that preparations enriched in c9, t11, and t10, c10 isomers are preferable. Although CLA is generally safe, its use in patients with chronic conditions such as diabetes should be monitored more closely as CLA has been reported to increase insulin resistance.

Green Tea Extract with or without Caffeine
There are numerous catechins found in green tea extract, the most important of which is believed to be epigallocatechin gallate (EGCG) which is involved in the inhibition of adipocyte differentiation and proliferation, reduced fat absorption, inhibition of catecho-o-methyl transferase, increased energy expenditure and increased utilization of fat. It also has natural caffeine which has been reversibly associated with weight gain probably due to its known thermogenic effects and increase energy expenditure. In a systematic review and meta-analysis which evaluated data from 15 trials it was reported that over a 12-week period those who ingested a median of 588mg daily of green tea catechins (GTCs) with caffeine compared with dose who drank caffeine alone had a statistically significant weight loss of around 1.38kg and an average reduction in waist circumference of 1.93 cm. A statistically significant 0.44 kg weight loss was observed in a group of individuals ingesting GTC with caffeine compared to a caffeine free control group. These results seem to indicate that there is synergism between GTC and caffeine, as studies evaluating GTC administration on its own showed no benefits in weight loss. Safety concerns with GTCs are minimal; although there were some reports of liver dysfunction, these were not sustained when investigated for short-term use. Yet the authors of this meta-analysis stated that despite the significant results, for pharmacologic weight loss products, patients are considered to have failed treatment if they have not achieved a loss of 2 kg after 4 weeks of therapy, which as one can deduce, is well beyond the results provided with GTC and caffeine administration.

Garcinia Cambogia
Garcinia Cambogia is a tropical fruit high in hydroxycitric acid (HCA). There are various claims on how HCA actually causes weight loss, most of which come from animal studies. The most popular is that HCA inhibits the enzyme adenosine triphosphatase-citrate-lyase, which in laymen’s terms is the fat producing enzyme. Others report that HCA increases the release or availability of serotonin in the brain, thus leading to appetite suppression. Other theories on its mechanism of action include the inhibition of pancreatic alpha amyrase and intestinal alpha glucosidase responsible for carbohydrate metabolism. In a systematic review published in Journal of Obesity, the authors concluded that the overall efficacy is minimal to be of clinical relevance when taking into consideration well-designed human studies. It is also still undetermined what the recommended dose should be as it varied significantly from 1 g to 2.8 g daily. Duration of treatment is also uncertain and could be limited by adverse effects such as gastrointestinal disturbances and headaches. In summary, it seems that although some studies have shown that HCA may generate weight loss, this is too minimal for recommending it to the general public and more research is necessary.

Guarana
Guarana is a plant which contains caffeine, theophylline and theobromide and thus has been incorporated as a stimulant into weight loss and nutritional supplements as it enhances athletic performance and reduces mental and physical fatigue. There are no studies which have looked at the isolated effect of guarana however there are studies in combination with yerba mate, Ma Huang (ephedra) and Damiana. In a small study in combination with Ma Huang, it was found that over an eight-week period, subjects had an average weight loss of 4 kg compared to the group receiving placebo, with minimal adverse symptoms reported. In a double-blind randomised trial study investigating a product containing extracts of Yerba Mate, Guarana and Damiana for 45 days, researchers reported a weight loss of 5.1 kg compared with only 0.3 kg in the group given placebo. In a post-marketing research, a small group of 48 patients were followed up for 28 days and self-reported a mean loss of 2.3 kg in body weight. Although the loss in weight was significant the sample size were small and thus it is difficult to extrapolate the data to the general population, yet at least this combination seems to have some potential.

Orlistat
Orlistat is a specific, potent and long-acting inhibitor of gastrointestinal lipases. It forms a covalent bond with around 30% of the active serine site of gastric and pancreatic lipases inactivating them so that they are unavailable to hydrolyse dietary fat into absorbable free fatty acids and monoglycerides. Orlistat was originally marketed as a prescription only medicine (POM) but a few years later the reduced dose was available as an OTC preparation. In 2003 a Cochrane meta-analysis which included eight randomized double blinded trials revealed that the drug was modestly effective in promoting weight loss. An update review published a few years later concluded that orlistat was associated with a weight loss of around 3% more than diet alone in overweight and obese people. Orlistat 120mg administered three times daily contributed to a 2.7 kg weight loss more than diet alone. The period of time over which this loss was observed was not specified. In a 2014 meta-analysis which pooled data from 45 studies reported that patients on orlistat 120mg three times daily had a mean loss of 2.34 kg whereas patients on 60mg or 30mg three times daily had a mean loss of 0.7 kg. This loss was maintained after 18 and 36 months. Adverse events reported with orlistat are directly related to its mode of action and refer to gastrointestinal events. Orlistat was also studied in patients with type-2 diabetes and non-alcoholic fatty liver disease (NAFLD) with good preliminary results of
improvement in glycaemic control, lower cholesterol and blood pressure values. It is suggested that orlistat is only cost effective in those achieving at least 5% weight loss after 3 months and this is the same threshold the company adopts for cessation of treatment.

Conclusion
Most of the products available locally seem to contain different dosages of a number of the above mentioned ingredients, some even combined with other ingredients. It is difficult to say whether combining such ingredients would have an additive or synergistic effect or whether this would mean having more significant adverse events. Most of the studies on individual preparations seem to be flawed in their design and usually come from the company marketing the product which introduces an element of bias. As health care professionals we need to offer the correct advice being mindful that the product may provide minimal benefit.

Key points
- To lose one kilogram (kg) in body weight there has to be a deficit of approximately 7,000 kilocalories.
- Most weight loss products available on the market lack rigorous evidence to back up their claims.
- Weight loss products should always be recommended as an adjunct to healthy diet and regular exercise.
- Low-dose orlistat is the only OTC preparation approved by the Food and Drug Administration and the European Medicines Agency available in Malta.
- Extra caution needs to be taken in patients who are overweight or obese and who have additional co-morbidities such as diabetes and cardiovascular events, since most of the products reviewed below have not been investigated in these populations.

References
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